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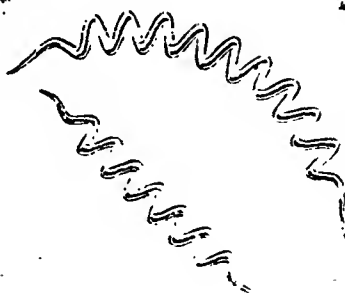
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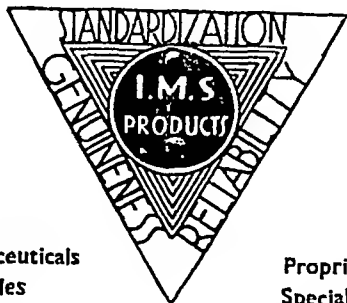
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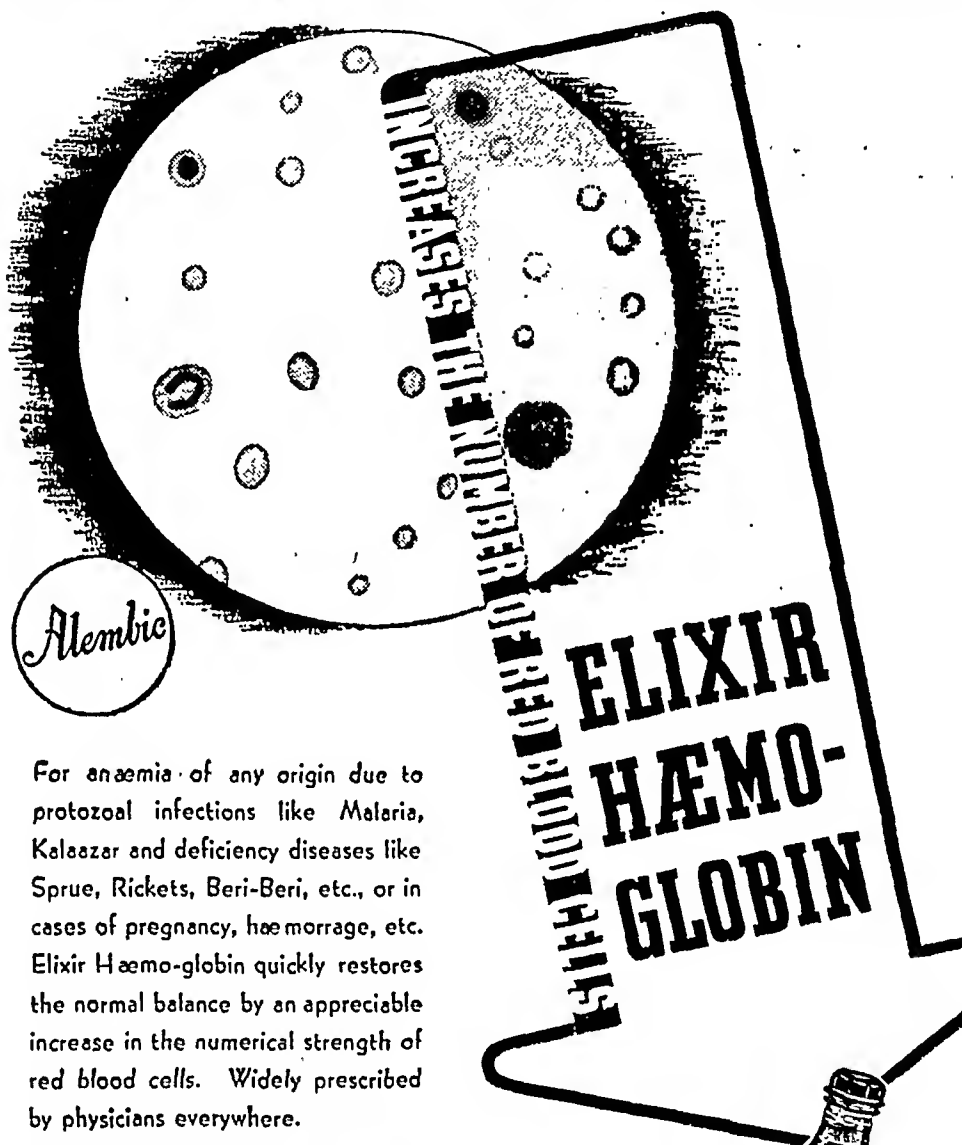
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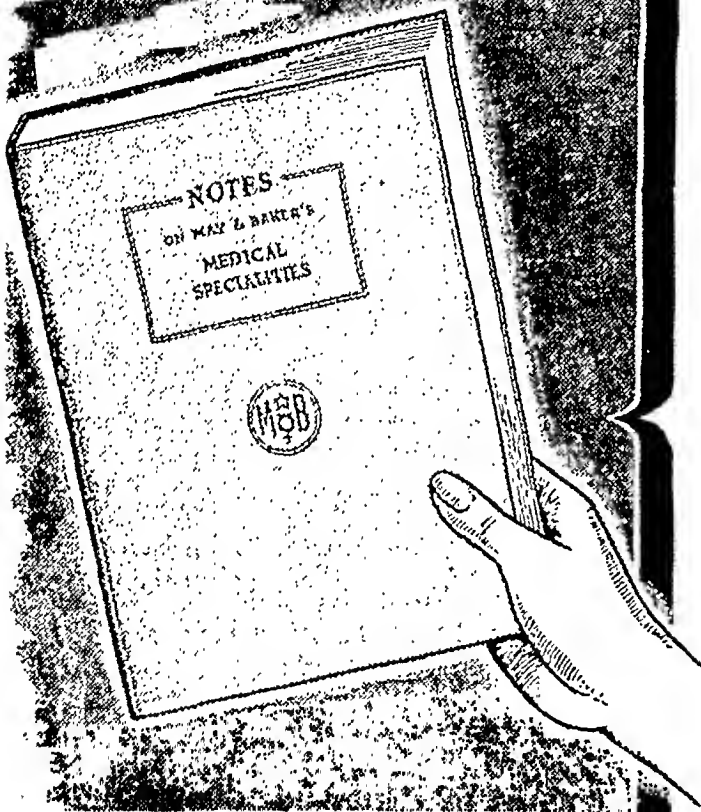
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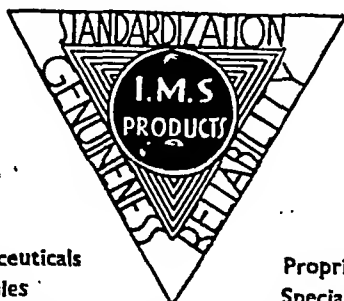
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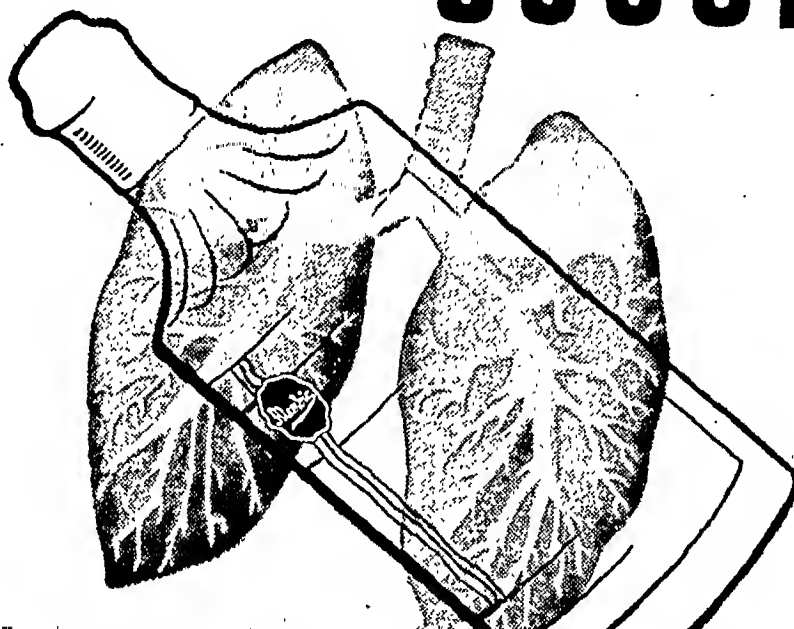
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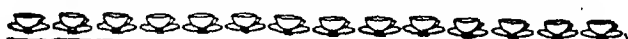
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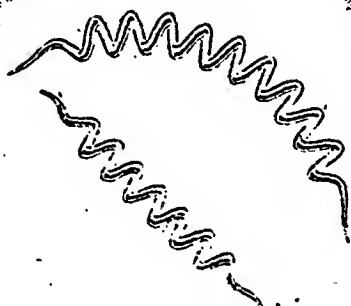
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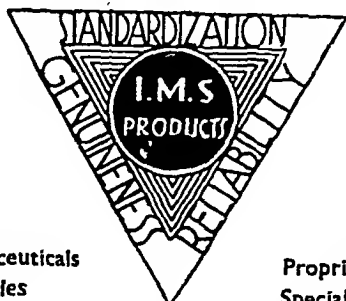
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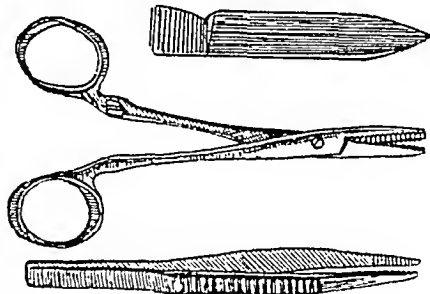
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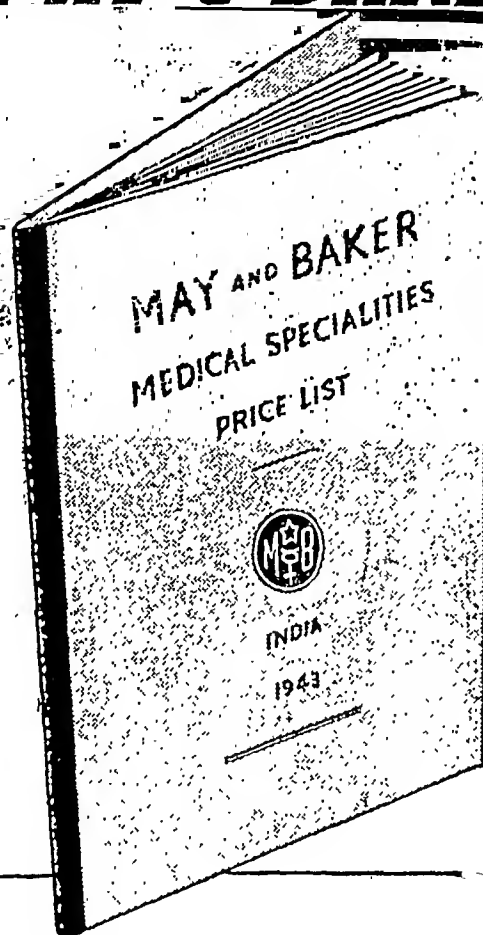


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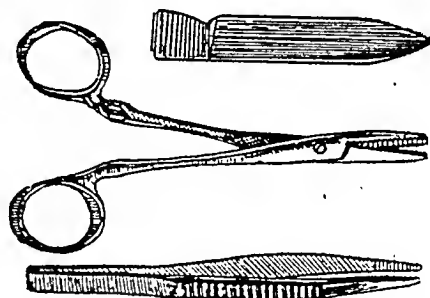
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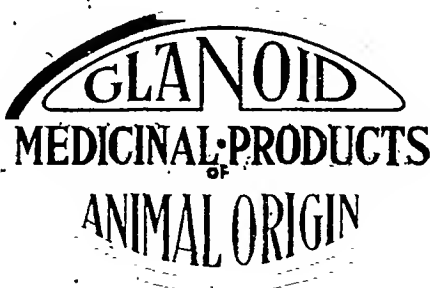
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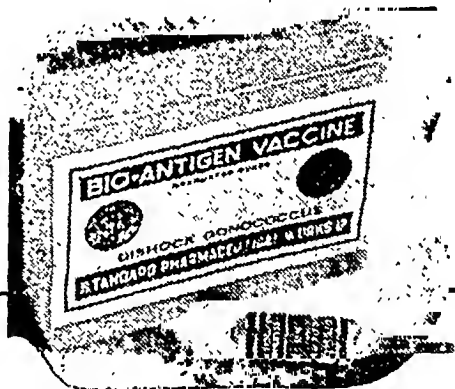
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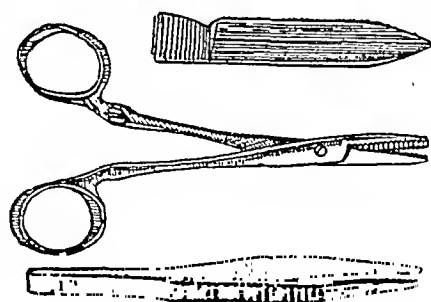
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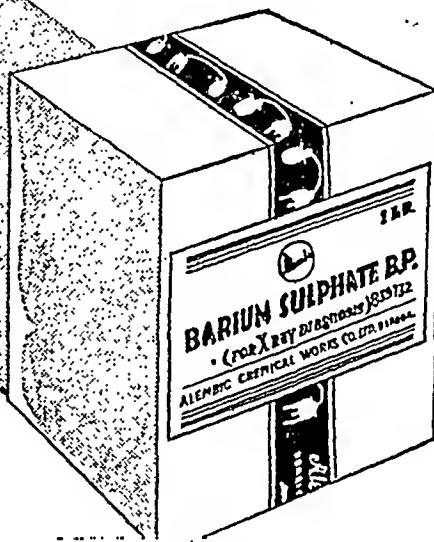
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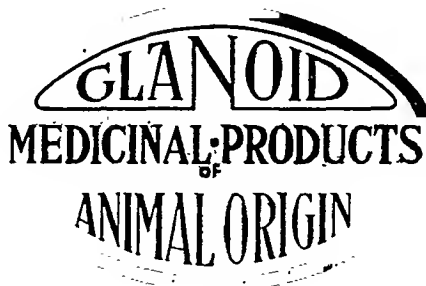
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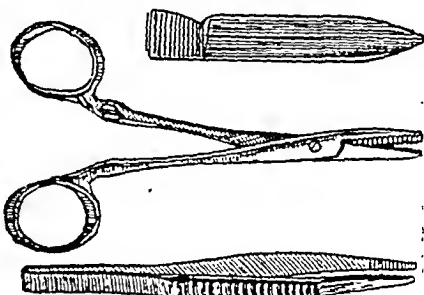
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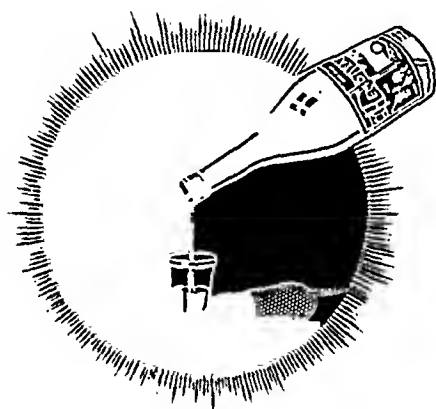
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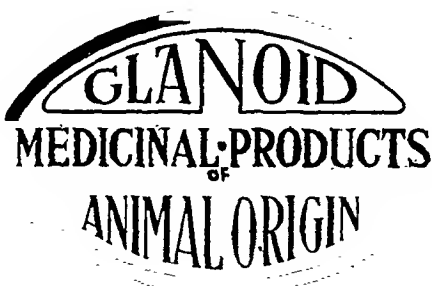
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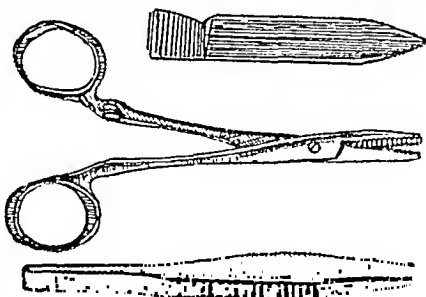
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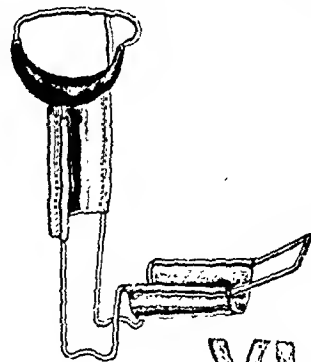
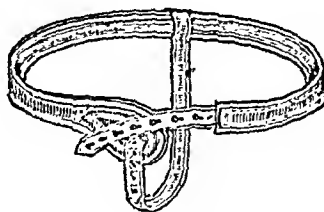
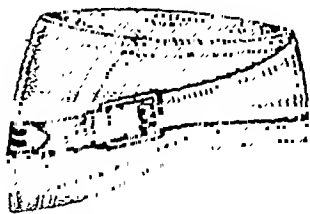
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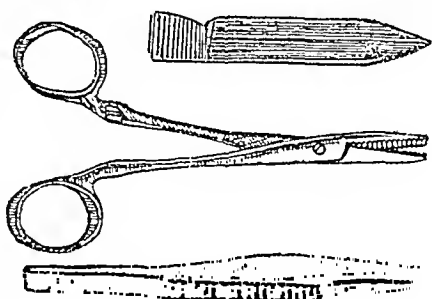
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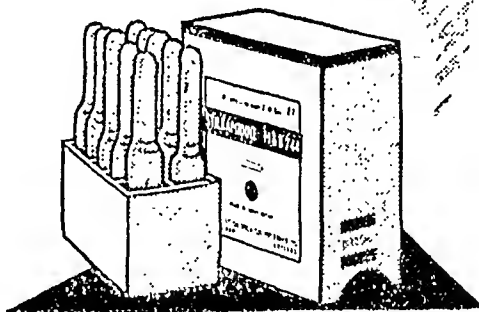
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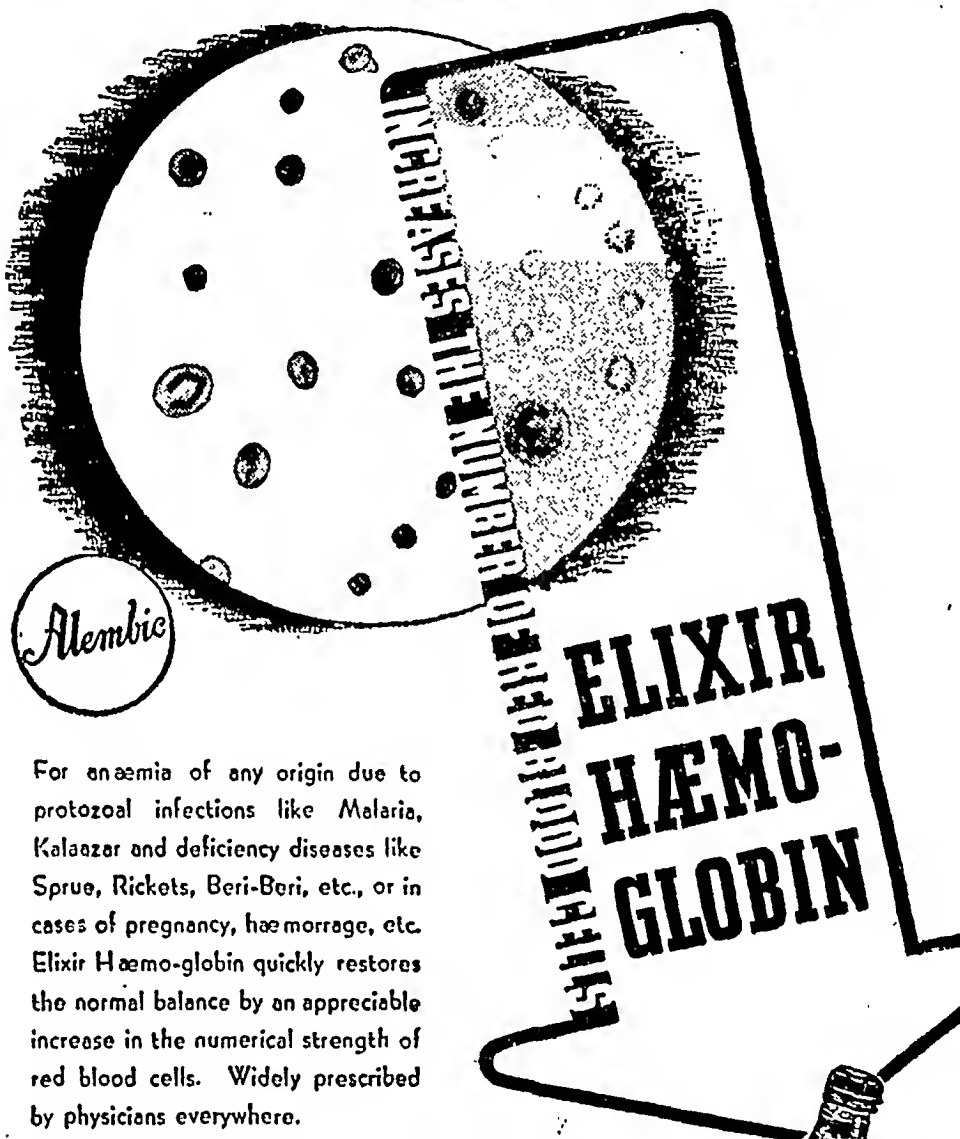
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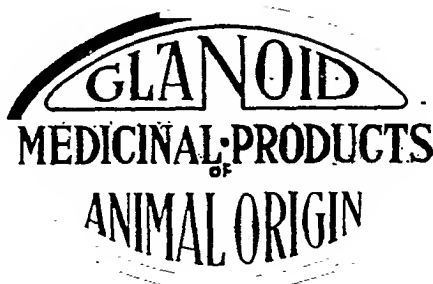
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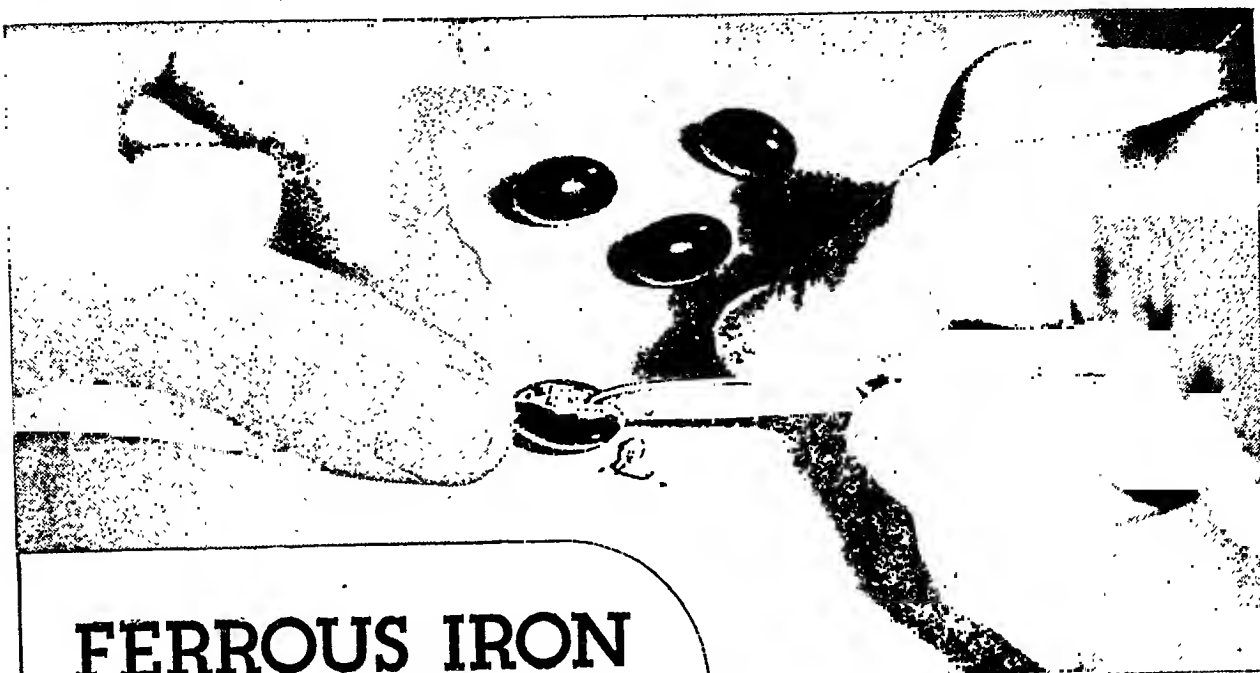
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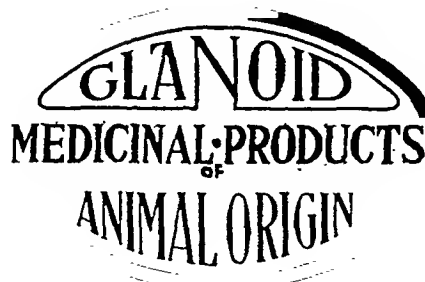
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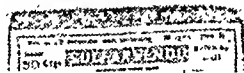
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Original Articles

ACUTE MONOCYTIC LEUKÆMIA IN INDIANS

By L. EVERARD NAPIER, C.I.E., F.R.C.P. (Lond.)
C. R. DAS GUPTA, M.B. (Cal.), D.T.M.

and

P. C. SEN GUPTA, M.B. (Cal.)

(From the School of Tropical Medicine, Calcutta)

Introduction.—Monocytic leukæmia was first described by Reshad and Schilling-Torgau in 1913. Ever since its first description, it has been a subject of controversy. The controversy has centred round the question whether or not it is a disease entity, distinct from the other two types of leukæmia, *viz*, myeloid and lymphatic, and much confusion has resulted from the disagreements regarding the origin of monocytes, and from the use of different names by various authorities to indicate this condition. At the present time, the monocytes are regarded as an independent line of cells, distinct from granulocytes and lymphocytes, and monocytic leukæmia is accepted as a clinical and hæmatological entity, though a considerable degree of disagreement in nomenclature still remains, which is largely dependent on the difference of opinion regarding the relation of the monocyte to the reticulo-endothelial system.

Monocytic leukæmia is much less common than the myeloid and the lymphatic varieties. Rosenthal and Harris (Forkner, 1938) in an analysis of 455 cases of leukæmia found 1.5 per cent cases to be acute and 0.4 per cent chronic monocytic leukæmia. The actual incidence of monocytic leukæmia is difficult to estimate, as most of the cases are acute and are very often unrecognized or confused with other types of leukæmia. Forkner (1939) suggests that about 5 to 15 per cent of acute leukæmia are monocytic in type.

Almost all cases of monocytic leukæmia reported are from the white races; only two cases have been reported in Chinese and one suspicious case in an Indian by Wright (Forkner, 1938). Within a period of 15 months (1937-39) we encountered three cases that on hæmatological investigation proved to be acute monocytic leukæmia, and recently a fourth such case came under our observation: all the patients were Indians. The notes of one of the cases were given in the *Annual Report of the Calcutta School of Tropical Medicine, 1937*. The notes on these four cases are given below.

Case I.—R. N., a Bengalee Hindu male, aged 16 years, was admitted on 11th June, 1937, in the hospital of the Calcutta School of Tropical Medicine, for irregular attacks of fever, progressive weakness, anæmia, jaundice and chronic cough. The fever started about three months previous to admission and had never been very high. With the persistence of the fever, the patient became progressively weak and

anæmic, and jaundice was noticed about a month after the onset of fever.

Past illness.—He had enteric fever 13 years ago, kala-azar 12 years ago, and occasional attacks of malarial fever; he had epistaxis two years ago. The family history did not reveal anything of importance.

On admission, the patient was found to be very anæmic and there was a moderate degree of jaundice. The heart was enlarged, the apex beat being about half an inch beyond the nipple line; there was a systolic bruit in the pulmonary and mitral areas, which was apparently hæmic in origin; and the pulmonary second sound was accentuated. The lungs did not show any abnormality. The liver was enlarged $\frac{3}{4}$ inch and the spleen $1\frac{1}{2}$ inch below the costal margins. There was no other abnormality.

The result of the routine examination of blood, sternal puncture material, urine, fæces, etc., are given below.

Blood: Wassermann reaction—slightly positive; bacterial culture—*nil*; malarial culture—*nil*; leishmania culture—*nil*; aldehyde reaction—(+); coagulation time (bead method)—3 mins. 25 secs.; bleeding time—5 mins. 30 secs.; malarial parasites—none found; microfilaria—none present; grouping test—group B.

The mean corpuscular volume was 102.6 cu. μ , the mean corpuscular hæmoglobin 27.5 $\gamma\gamma$, and the mean corpuscular hæmoglobin concentration 26.8 per cent, the direct van den Bergh reaction gave a delayed positive reaction on 12th June: the other blood findings are shown in table I, on the next page.

The urine examination on admission showed a marked increase of urobilin and the presence of bile pigment as the only abnormalities.

In the stools, scanty giardia cysts, a few hookworm ova (less than 100 per gramme), and ascaris ova (700 per gramme) were found.

Scrapings from the face and neck showed *Malassiezia furfur* (*Tinea versicolor*) and the skiagram, marked general cardiac enlargement and congestion of the lungs.

The patient was first put on a cholagogue mixture with hexamine. As the blood examination showed macrocytic anæmia, liver extract (P. D. and Co.) 2 c.cm. daily for 5 days and campolon 2 c.cm. daily for 5 days were given. The liver therapy was however unsuccessful in causing any improvement in the anæmia which progressively increased. The fever also persisted and by 26th June he had developed œdema of the face and legs. On the 1st July, he complained of the dimness of vision in the right eye. Ophthalmoscopic examination revealed leukæmic retinitis. Examination of the blood on the 3rd July showed that the red cells were below one million, and blood transfusion was decided upon. A blood transfusion was given on 9th July. The amount transfused had to be restricted to 9 ounces only, there being a marked dilatation of the heart and a rapid pulse rate. Even with this transfusion the patient had a sharp reaction; he had a rigor and his temperature went up to 105°F., but subsided in a few hours. There was slight improvement of anæmia but it was only temporary and during the next fortnight the anæmia progressively increased.

Deep x-ray therapy was not considered to be advisable on account of severe anæmia and also of the fact that in acute cases it is not usually a successful therapeutic measure. Four injections of cobra venom were given, empirically, on the hypothesis that the leukæmia is a neoplastic process and that cobra venom is said to be useful in some types of new growth. This proved to be of no value.

The general condition of the patient was growing progressively worse. The temperature was of low remittent type throughout. The anæmia was progressively increasing and marked œdema of the legs and face and slight œdema of the whole body had developed. The size of the spleen had increased to 3 inches below the costal margin. The heart was greatly dilated, the apex beat reaching the anterior axillary line and the right border about an inch outside the sternum. The patient developed gallop rhythm on the 11th July. This persisted for 3 or 4 days. On

the 14th, he had an attack of hæmatemesis. He developed orthopnoea about this time, and the pulse rate was between 120 and 140 per minute and the respiration rate between 36 and 40 per minute. On the 16th and 17th July, he had hæmoptysis. Besides the usual treatment of hæmorrhage, a course of injections of cebion (vitamin C) was given. Though the patient did not have any further hæmorrhages, the general condition became rapidly worse, and he developed œdema of the legs on the 29th July, and died on the same day, with increasing anæmia, orthopnoea, tachycardia, and subnormal temperature.

evening. The temperature continued to be high and the patient had attacks of vomiting. He next complained of defective vision; ophthalmoscopic examination revealed patches of hæmorrhage all over the fundi with early retinitis in both eyes. He left hospital on 21st February, 1938.

After leaving the hospital the patient was under our observation and was treated symptomatically. The temperature gradually came down. As the anæmia was becoming severe, he was given a small blood transfusion (8 ounces) on 8th March. The temperature became normal from the next day, and the patient was

TABLE I showing the findings in the peripheral blood and sternal puncture material in case I

Date	Hæmoglobin	Red blood cells	Reticulocytes, per cent	Nucleated cells, per c.mm.	Megaloblast	Erythroblast	Normoblast	Monoblast	Large mononuclears	Lymphocyte	Myeloblast	Premyelocyte	Neutrophil myelocyte	Young neutrophil	Band neutrophil	Segment neutrophil	Eosinophil	Van den Bergh indirect test, bilirubin units
1937																		
12th June	4.675	1,700,000	32.6	24,200	Nil	Nil	62	23.5	2	1.5	Nil	Nil	Nil	Nil	2	4.5	4.5	5
21st June	3.7125	1,100,000	49	31,500	Nil	Nil	71.5	12	2	4.5	Nil	Nil	Nil	Nil	3	4	3	4.5
28th June	3.575	1,080,000	58	58,700	1.5	0.5	75.5	6	4.5	3.5	Nil	Nil	Nil	Nil	1	6	1.5	3.5
3rd July	2.75	720,000	39.8	22,000	0.5	1.5	75.5	6	4	8	Nil	Nil	Nil	Nil	4.5	6	1.5	4.0
7th July	3.85	1,260,000	26.6	38,000	Nil	0.5	69.5	6	4	3	Nil	Nil	Nil	Nil	4.5	6	6	2.2
12th July	3.025	1,000,000	15.8	10,000	0.5	1.5	59.5	10	7	3	Nil	Nil	Nil	1	4.5	6	3	..
22nd July	2.75	705,000	16.3	8,250	Nil	1	58.5	4.5	6	14.5	Nil	Nil	Nil	Nil	4.5	8	3	..
Sternal puncture																		
15th June	3.755	1,460,000	30.2	73,200	0.8	5.2	25.2	20.8*	10.4	11.2	0.8	0.8	Nil	Nil	8.4	2	2	..

* plus 12.4 premonocytes.

Case II.—S. K. M., Bengalee Hindu male, aged 27 years, of average build (weight 156 lb.) was admitted on 2nd February, 1938, for periodic attacks of fever since 26th December, 1937. The first attack of fever lasted for 2 days. Since then, the patient had been getting attacks of fever lasting 2 to 3 days almost every week during January 1938. A blood count was done outside and a diagnosis of acute leukaemia (lymphatic) made.

On admission, the patient was found to be anæmic; the tongue was coated but no sores were present in the mouth or throat; pulse rate 120; temperature 99°F. The liver and the spleen were not enlarged and no abnormality was detected in the lungs, heart, or other organs.

Laboratory investigation.—For sternal puncture and blood count—see table II. The urine showed no abnormality except the presence of excess of urobilin and of indican. Stool examination—no abnormality; aldehyde and antimony tests—negative; Wassermann reaction—negative; van den Bergh test, direct and indirect—negative; blood group 'O'.

Skiagram of chest.—An apparently normal chest: no evidence of lung infiltration. The root shadows a little heavy and there were a few calcified spots in the upper peri-hilar regions on both sides, possibly due to healed infantile infection.

After admission the patient was put on hæmatinics, viz, campolon and marmite. The general condition was fair, and the temperature varied between 98°F. and 99°F., but no improvement took place in the blood condition. About a fortnight after admission, he was complaining of a slight defect in hearing and throbbing of the head. Two days after this, the temperature rose to 100°F. in the evening. He was given a deep x-ray exposure on the next day, and there was a sharp rise of temperature up to 103°F. with a rigor in the

feeling much better, but as anæmia was progressively getting worse, a second transfusion (18 ounces) was given. This led to a slight improvement in the anæmia and the total leucocyte count also fell below 30,000 per c.mm. The temperature remained at a low level (about 99°F.) until the 24th March, and there was relief of some of his symptoms, e.g., his irritable cough and the attacks of diarrhoea. The next bout of fever commenced on the 25th, after an injection of campolon, and lasted until the 3rd April, after which the temperature remained at a low level until the 18th April. During this period he felt slightly better, the hæmoglobin was about 5 gm. per cent, the red blood cells between 1.5 to 1.8 million per c.mm., and the white blood cells between 27 and 29 thousand per c.mm. The patient next had severe pain on the right side of the neck and discharge of pus from the left ear. The pain became localized in the neck and right ear, and he developed right-sided facial palsy. A myringotomy was done by a specialist, on the right ear, but no pus came out and there was no relief of symptoms.

The next bout of fever commenced on the 19th April, the temperature rising step-ladder fashion, but after a few days it came down by lysis reaching the level of about 99°F. on the 3rd May, and it remained about this level until the 23rd May. During this period, however, instead of slight relief of symptoms, complications appeared; there was repeated bleeding from the gums, bilious vomiting, and diarrhoea. The patient also complained of severe pain and tenderness over the 9th left rib. There was progressive increase of anæmia and he had hæmoptysis on 3rd May. A blood transfusion (20 ounces) caused slight improvement of the blood condition, but the other symptoms persisted. He still had bleeding from the gums, and later developed stomatitis; vomiting,

diarrhœa, discharge of pus from the ear, and hæmoptysis continued. About this time he complained of constant pulsation and tingling sensation in the head; the defect of vision persisted; the facial palsy on the right side was complete; and there was loss of taste on the right side of the tongue. The anæmia was profound (hæmoglobin 3.025 gm. per cent, red blood cells 1.0 million per c.mm.). The heart was dilated and there were marked hæmic bruits. The liver was now enlarged to half an inch below the costal margin and was tender. Except for a small submaxillary gland no enlargement of the lymph glands was present. The fever commenced to rise on the 23rd; by the 27th it had reached 104°F., and the patient was gravely ill, he was vomiting almost after every feed, and was restless and sleepless. He had intense pruritis ani which had to be relieved with cocaine.

He died on the 28th May, being conscious almost to the end.

was much enlarged, the lower border being midway between the umbilicus and the pubis; and hard. There was a hæmic murmur over the heart; the testes were hard and enlarged.

Laboratory investigations.—For blood counts—see table III. Urine—no abnormality; stools—no ova, protozoa, cysts or pathogenic bacteria found; Widal reaction—negative; aldehyde test—negative; Chopra's test—positive; bleeding time—3 mins. 20 secs.; coagulation time—4 mins. 35 secs.; fragility—hæmolysis commences at 0.34 per cent NaCl, not completed in the other tubes. Platelet count—180,000 per c.mm. 12th December, 1938: reticulocyte—3.5 per cent. Throat swab culture—*N. catarrhalis*, *strepto. viridans*, and pneumococci. No *C. diphtheriæ* found.

After admission, his temperature began to rise step-ladder fashion, reaching the maximum about the sixth day. It started to come down after the next 3 days, and it was normal on the twelfth day of his

TABLE II (case II)

Date	Hæmoglobin, gm. %	RBC in millions	Reticulocytes % of RBC	MCV	MCH	MCHC	Nucleated cells in 10 ³	Normoblast	Monoblast	Premonocyte	Monocyte	Lymphocyte	Eosinophil	Myelocyte neutrophil	Myelocyte eosinophil	Neutrophil young forms	Neutrophil band forms	Neutrophil segment forms	Plasma cell	Others
<i>Sternal puncture</i> 4-2-38	8.38	2.51	1.7	99.7	4.0	70.0	5.6	5.2	3.2	2.4	0.4	0.8	0.4	5.2	2.8	+	?R.E. cell +
<i>Blood</i>																				
2-2-38	2.0	80.4	1.2	1.2	3.6	0.4	0.0	0.0	0.4	3.2	7.6	..	?
9-2-38	43.2	1.2	75.2	5.2	2.0	8.0	0.8	5.2	4.4	..	R.E. cell +
14-2-38	8.25	2.25	0.8	43.8	4.8	74.8	2.0	0.4	6.4	0.8	6.8	12.0
21-2-38	5.775	1.75	1.3	97.1	33.0	33.9	78.0	2.0	58	7.2	5.2	6.0	5.2	16.4	..	?
26-2-38	4.67	1.35	70.0	2.0	82	3.2	1.2	3.6	0.4	1.6	5.6	..	R.E. cell 0.4
3-3-38	4.26	1.30	0.8	50.0	1.2	78.4	2.0	4.8	2.4	3.2	0.4	2.4	4.4	0.8	..
10-3-38	4.80	1.61	0.6	27.0	4.4	42.0	0.8	7.2	6.0	0.4	4.4	13.2	21.2	..	Basophil 0.4
26-3-38	4.4	1.41	1.1	88.6	31.2	35.2	6.7	3.0	16.0	1.0	3.0	7.0
2-4-38	5.08	1.36	1.4	117.6	37.3	31.7	28.3	1.0	61.0	8.0	..	10.0	0.8	3.0	4.8
9-4-38	5.08	1.44	1.3	97.2	35.2	36.2	26.9	2.0	72.8	6.8	1.6	10.0	0.8	0.4	..	0.4	0.4	4.8
19-4-38	5.625	1.80	2.6	38.0	6.0	61.6	5.2	4.0	9.2	0.4	0.0	..	0.8	5.6	7.2
25-4-38	4.53	1.15	0.9	64.5	1.6	68.8	4.8	2.8	3.6	0.4	7.6	10.0	..	R.E. cell 0.4
2-5-38	3.71	0.92	..	119.5	40.3	33.7	27.0	3.2	58.8	9.2	6.8	6.4	1.2	5.2	8.8	..	R.E. cell 0.4
9-5-38	5.6	1.36	0.5	12.8	2.8	45.6	2.8	10.0	18.4	0.8	8.0	11.6
18-5-38	4.67	1.27	0.3	9.0
25-5-38	3.025	1.00	0.2	120.0	30.25	25.2	21.8	5.2	61.2	5.6	1.6	13.2	7.2	6.0

R.E. cell = Reticulo-endothelial cell.

Case III.—A Bengalee Hindu male child, aged 6 years, was admitted in the children's ward, Medical College Hospital, on 26th August, 1938, under Major Kelly for the following complaints. Irregular fever, enlargement of the glands in the neck and groin, wasting and anæmia for about one and a half months, enlargement of the spleen for one month, and a slight evening rise of temperature. On admission, the patient was found to be anæmic; there was ascites; the cervical, pre-auricular, and inguinal glands and the submaxillary salivary glands were enlarged, firm, and discrete. The pulse was 110 per minute and the respiration 26 per minute; the liver was enlarged one finger's breadth below the costal margin; the spleen

stay in hospital (5th September). The next bout of fever started on the following day, and showed a gradual rise to the fastigium. This attack was more prolonged, lasting about 20 days. The temperature did not however come down to normal, but remained between 98.4 and 100.6 for the next 6 days (26th September to 1st October). The next bout of fever lasted about 11 or 12 days. Then an apyrexial period of 11 days (13th October to 23rd October) was followed by a febrile period of 3 days. The patient was afebrile for the next 2 days. The next bout of fever lasted 35 days (29th October to 2nd December), the temperature gradually rising and then remaining remittent almost to the end of this period. The temperature

remained about 99°F. for a day after this, and then the terminal attack of fever commenced. This bout of fever lasted 20 days. (The patient died with a temperature of 105°F. on the 22nd December, 1938.)

The patient's general condition improved to some extent during the apyrexial period towards the end of October, but with the recurrence of fever his condition became progressively worse. There was gradual increase of oedema with the decline of general health. The anaemia improved to some extent with blood transfusion and hæmatinics, and about the end of October the hæmoglobin was 60 per cent and the red cells 3.12 millions. After this there was a progressive increase of anaemia. The patient developed jaundice, obstructive in type (van den Bergh direct—immediate + bilirubin 26 units), a few days after the blood transfusion. This cleared up very gradually. The liver gradually enlarged and before the fatal termination it was 3 inches below the costal margin. There was no further enlargement of the spleen or of the glands. The patient had swelling of the elbow and knee joints (? synovitis) early in October. This persisted for about a fortnight. He (early November) showed signs of periostitis of the lower $\frac{1}{4}$ of the ulna, and irregular swellings over the left side of the head and the left mandible. The periosteal involvement of the ulna gradually subsided but the latter became more prominent with the progress of the disease.

His pulse rate remained between 110 and 120 per minute and from the second week of December it was between 140 to 160 per minute.

The patient had bleeding from the gums 3 days previous to his death.

The treatment adopted was mainly administration of hæmatinics, ferri et ammonii citras, and liver extract by mouth and also parenterally. The patient was given a blood transfusion (4½ oz.) soon after admission (3rd September). This caused a sharp febrile reaction. Besides this, symptomatic treatment for various complications, such as periostitis, joint involvement, cardiac insufficiency, etc., was carried out.

TABLE III showing blood findings in case III (Medical College Hospital)

Date	Hæmoglobin per cent, Tallqvist's scale	Red cells in millions per c.mm.	White blood cells in thousands per c.mm.
25-8-38	35	1.64	34.9
6-9-38	40	1.80	..
26-9-38	55	2.45	12.48
7-10-38	60	3.10	11.2
26-10-38	60	3.12	20.0
9-11-38	55	2.94	23.0

20-12-38. Differential count (our interpretation)

Monoblasts	.. 62.8	Basophils	.. 0.4
Premonocytes	.. 4.4	Myelocytes	.. 1.2
Monocytes	.. 5.6	Neutrophils—	
Lymphocytes	.. 4	young	.. nil
Plasma cells	.. 1.6	band	.. 9.6
Eosinophils	.. 4	segment	.. 5.6
		Normoblasts	.. 0.8

Case IV.—S., a Bengalee Hindu boy, aged 12 years, attended the hæmatological clinic, Calcutta School of Tropical Medicine, on 4th September, 1942, for low remittent pyrexia, gradual loss of weight, and progressive anaemia, for about six months.

On examination, the patient was found to be profoundly anæmic and emaciated. There was slight puffiness of the face and oedema round the ankles. There was a swelling of the forehead (over the region of the frontal sinus) and of the maxillæ, more on the left side. The left eye showed a slight degree of

exophthalmos. On opening the mouth, the swelling of the maxillary antra was seen to cause a bulging into the mouth. The gums were spongy. The inguinal lymph glands were enlarged, more markedly on the left side. The liver and the spleen were not enlarged. No other marked abnormality was noted. The patient was lost sight of after the hæmatological investigations were completed.

Blood count, 4th September, 1939. Hæmoglobin—5.08 gm. per cent; red blood cell—1.29 million per c.mm.; reticulocytes—7 per cent of red blood cell; mean corpuscular volume—131.7 cu.μ; mean corpuscular hæmoglobin—39.5 γγ; mean corpuscular hæmoglobin concentration—29.8 per cent; leucocytes—18,550 per c.mm.; neutrophil—10 per cent; lymphocyte—16 per cent; monoblasts, premonocytes and monocytes—71 per cent; eosinophil—3 per cent.

TABLE IV showing differential count of sternal puncture material of case IV

	Per cent
Red cell series	5.8
Megaloblast	nil
Erythroblast	nil
Normoblast	5.8
White cell series	94.2
Myeloblast	nil
Premyelocyte	nil
Neutro. myelocyte	0.4
" metamyelocyte	0.4
" band forms	2.4
" segment forms	0.2
Eosino. myelocyte	0.4
" metamyelocyte	nil
Band forms	0.2
Segmented forms	0.2
Basophil	0.2
Lymphoblasts	nil
Lymphocyte	3.4
Plasma cell	nil
Monoblast	84.0
Premonocyte	1.0
Monocyte	1.0
Megakaryocyte	nil

A summary of the chief hæmatological findings is given in table V, below. It will be seen that the anaemia was macrocytic in type in three of the cases. In case I, the anaemia was hæmolytic in type. The leucocyte count was not very high in any case and most cases passed on to the sub-leucoerythæmic stage during the course of the disease.

The differential count of the peripheral blood showed an overwhelming preponderance of monoblasts and premonocytes with a few monocytes in all cases. In all the cases a few mature myelocytes were found in the peripheral blood. The examination of the sternal marrow revealed that monoblasts, premonocytes, and monocytes had replaced most of other elements in the marrow. Only in case I was there some evidence of erythropoiesis in the marrow.

Discussion.—Recognition of the type in acute leukaemia is regarded, and rightly so, as very difficult. The clinical pictures presented by the three principal types are so similar to each other that a clinical diagnosis of the type

TABLE V

BLOOD		Case I	Case II	Case III	Case IV
Hæmoglobin in gm. %	{ Initial Final	4.67 2.75	8.25 3.025	? ?	5.08 ..
RBC in millions per c.mm.	{ Initial Final	1.70 0.705	2.25 1.0	1.64 ..	1.29 ..
Reticulocyte (% of RBC)	..	32.6	0.8	3.5	7.0
Mean corpuscular volume (cu. μ)	..	102.6	120.0	..	131.7
Mean corpuscular hæmoglobin ($\gamma\gamma$)	..	27.5	30.25	..	39.5
Mean corpuscular hæmoglobin conc. (%)	..	26.8	25.2	..	29.8
Van den Bergh test	Hyperbilirubin-æmia.	Negative	Obstructive jaundice at one period.	Negative
Type of anæmia	Macrocytic hæmolytic.	Macrocytic	..	Macrocytic
Leucocytes in thousands per c.mm.	{ Maximum Minimum	58.7 8.25	78.0 6.7	34.9 11.2	18.5 ..
Monoblasts, premonocytes and monocytes % (maximum).		25.5 (67.1% of WBC)	82.4	72.8	71.0
STERNAL BIOPSY					
Monoblasts, premonocytes and monocytes, per cent.		44.4	80.8	..	86.4
Cells of granulocyte series, per cent		13.2	12.0	..	4.4
Lymphocytes, per cent ..		11.2	3.2	..	3.4
Erythropoietic cells, per cent ..		31.2	4.0	..	5.8
Nucleated cells per c.mm. (in thousands).		73.2	99.7

can hardly be made with any degree of certainty. This fact and the fact that all cases are uniformly fatal has led many authors to feel that differentiation is unnecessary; this

attitude can hardly be regarded as likely to advance the cause of science.

The following table (VI) gives a summary of the principal clinical features of the cases :—

TABLE VI

	Case I	Case II	Case III	Case IV
Age in years ..	16	27	6	12
Duration in months	3	6/4	6/4	7/6
Fever	Low remittent	Pel-Ebstein type	Periods of high remittent pyrexia alternating with short low pyrexial or apyrexial periods.	Low remittent
Signs of involvement of bucco-pharyngeal mucous membrane.	Not marked, except bleeding gums.	Stomatitis and gingivitis short time before the fatal termination.	Not marked, bleeding gums.	Spongy gums
Liver enlargement below costal margin.	3"	0, later 1½"	1½", later 3"	Not enlarged
Spleen enlargement below tip of 9th left rib.	1½", later 3"	Not enlarged	Enlarged up to midway between umbilicus and pubis.	Not enlarged
Lymph glands ..	Not enlarged	Not enlarged except one small submaxillary gland.	Slight enlargement of cervical and inguinal glands, later becoming less prominent.	Inguinal lymph glands enlarged.
Bones and joints ..	No signs of involvement.	Pain and tenderness over 9th rib, left side.	Periosteal elevation over left ulna, swelling on left temporal bone and mandible. Also synovitis.	Swelling involving the frontal sinus and maxillary antra.
Eye changes ..	Leukæmic retinitis	Leukæmic retinitis
Hæmorrhages ..	Bleeding gums, hæmatemesis, hæmoptysis.	Bleeding gums, hæmoptysis.	Bleeding from the gums	..
Total duration (approximate) in months.	4½	5	5½	Not known

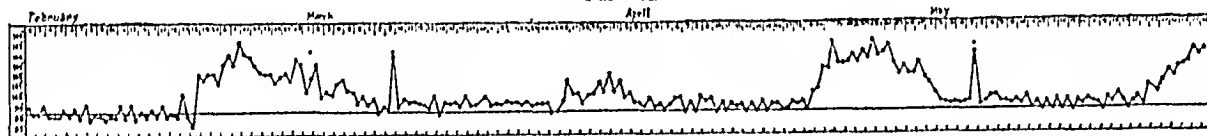
Other writers have made attempts to distinguish between the various types of the disease. Gilbert and Emile-Weil (1899: 1904) distinguished three principal types of acute leukaemia according to the prevalence of the main symptoms, (i) characterized by enlargement of lymph glands, (ii) the hæmorrhagic form, and (iii) the anginous or pseudo-scorbutic form. Forkner, as a result of intensive study of numerous cases of acute leukaemia and the correlation of clinical, hæmatological and histological data, arrived at what he regarded as distinct syndromes characteristic of acute lymphogenous, acute myelogenous, and acute monocytic leukaemia. He found that the first type of Gilbert and Emile-Weil corresponded to acute lymphatic, the second to acute myeloid and the third to acute monocytic leukaemia. He (Forkner, 1934) published in tabular form the main clinical and hæmatological differentiating features of the three types of acute leukaemia. Forkner always insisted on the importance of the lesions of bucco-pharyngeal mucous membrane in differentiating acute monocytic leukaemia, but other authorities (Whitby and Christie, 1935) do not attach so much importance to this feature. Also these peculiar oral lesions were found by Forkner himself in two patients with chloroleukaemia. So at the present time the tendency is to base the diagnosis more on the hæmatological picture than on the clinical features.

From a study of the summary of the chief clinical features of the cases reported above, it will be seen that there was hardly any similarity of clinical picture between the cases, and very slight resemblance to the types described by Gilbert and Emile-Weil and Forkner. The stomatitis and slight gingivitis that were seen in some of the cases had but little resemblance to that described by Forkner (1938) as diffuse marked swelling of the mucous membrane, particularly of the gums, usually with ulceration and necrosis, which he considered characteristic of acute monocytic leukaemia.

he called aleukæmic reticulosis—a condition which in his opinion was a distinct entity and related to monocytic leukaemia, in the same way as aleukæmic, lymphatic and myeloid leukaemia are related to lymphatic and myeloid leukaemia, respectively. This patient had the Pel-Ebstein type of fever, progressive anæmia, thrombocytopenia, leukopenia with normal proportions of the cells in the differential count. Biopsy of bone marrow and post-mortem examination revealed proliferation of reticulo-endothelial cells in the lymph nodes, spleen, bone marrow, liver and other organs. Giant cells of the Sternberg-Reed type were very numerous, few eosinophils were present and reticulin fibres could readily be demonstrated.

We (Napier, Chaudhuri and Sen Gupta, 1937) reported a case which showed the Pel-Ebstein type of fever associated with slight enlargement of lymph nodes and spleen, anæmia and leukopenia, and which ended fatally. On histological examination of a lymph gland, mononuclear cells, 'lymphoid cells', multinucleate giant cells of the Sternberg-Reed type, fibroblasts, and many swollen reticular cells were also seen in this case, and the leukopenia was associated with a marked increase in the proportion of large mononuclear cells; the maximum reached was 57 per cent at the peak of the temperature. The histological pictures in these two cases are very similar and typical of Hodgkin's disease. Consideration of these two cases and the case of monocytic leukaemia (case II) makes one feel that there may be some grounds for the suggestion that the type of case reviewed by Dameshek represents the aleukæmic type of monocytic leukaemia, and the type represented by the previous case reported by us (Napier, Chaudhuri and Sen Gupta, *loc. cit.*), the subleukæmic type, and the present case (case II), the leukæmic type of monocytic leukaemia. Also Doan (1939) reported certain cases of chronic monocytic leukaemia in which histological examination of the lymph nodes showed a picture closely resembling Hodgkin's granuloma. These

CHART



Note.—Three sharp rises of temperature, each marked X, are due to blood transfusion.

In all the cases under review, the disease was associated with fever; probably it was the first noticed symptom. In two cases (I and IV) it was low remittent in type. The type of fever in one of the cases (case II) deserves comment. In this patient the fever was of the Pel-Ebstein type during the period the patient was under our observation. This type of pyrexia has apparently not been reported in monocytic leukaemia by any other writer. Dameshek (1933) described a case, and reviewed others, of a condition which

facts tend to show that the two conditions, Hodgkin's disease and monocytic leukaemia, are closely related. The histological basis of both these conditions is similar, *viz*, proliferation of reticulo-endothelial cells. There are many investigators who maintain that the tissue phagocyte (elasmatoocyte or reticulo-endothelial phagocyte) and the blood monocyte merely represent different functional stages in the life of the same cell strain, and this may eventually be found to be the case (Doan, *loc. cit.*).

Involvement of the bones was rather frequent in this small series of cases, three out of four cases showing evidence of such lesions. Periosteal elevation was found in one (case III) in the left ulna, and this patient also had swelling over the left temporal bone and the left side of the mandible. This patient also had effusion in the elbow and knee joints. Case II probably had a similar periosteal lesion on his rib. What exactly was the type of lesion in case IV it is difficult to say, because no skiagram could be taken. In this patient there was marked swelling in the region of the frontal sinus and the maxillary antra, the latter pushing

increase of the monocyte series of cells, together with a relative diminution of other types of cells, *viz*, erythroblastic cells, cells of the granulocyte series, and lymphocytes. To these four may be added (v) decrease of platelets, and (vi) increase of coagulation and bleeding time.

The difficulty in hæmatological diagnosis of acute leukæmia is due to the fact that the blood shows an overwhelming preponderance of 'blast' cells, and that few or no intermediate and mature forms of the type of cells are seen. It is ordinarily exceedingly difficult to determine whether the blast cells are lymphoblasts, myeloblasts, or monoblasts. Careful study of

TABLE VII

Staining method	Myeloblast	Lymphoblast	Monoblast
May-Grünwald or Giemsa stain.	Cytoplasm: pale blue, transparent. Nucleus—round or oval, very fine chromatin network, no nuclear membrane; several vacuole like nucleoli present. Auer's bodies occasionally present. Usually associated with myelocyte A, B and C of Sabin.	Cytoplasm: similar to myeloblast. Nucleus—round, oval or slightly indented, fine chromatin network nuclear membrane present, several nucleoli. No Auer's body present. Usually associated with mature lymphocytes, occasional myelocyte C of Sabin may be seen.	Cytoplasm: deep blue, opaque. Nucleus—round or oval, or elongated, seems to be folded on itself or deeply indented. Margins of the nucleus distinct, often shows coarser fibrillar material. Very few nucleoli present. Auer's body seen in some of the cells. Usually associated with premonocytes and monocytes, occasional myelocyte C of Sabin seen.
Sato and Sekiya peroxidase stain.	Many oxidase-positive cells with variable amount of fine to coarse granules.	No oxidase-positive cells	Many cells contain very fine oxidase-positive granules. Granules fewer and finer than myeloblasts.
Supra-vital staining with neutral red and Janus green.	Non-motile round cells; nucleus almost fills the cell, often indented. No neutral-red-stained structure. Very fine mitochondria usually scattered diffusely.	Non-motile round cell, central nucleus. No neutral red bodies, coarse mitochondria. Vacuoles. Numerous fine mitochondria evenly distributed.	Motile large cell irregular in outline due to pseudopodia formation. Nucleus on one side. A rosette of neutral red stain may be present or there may be scattered orange red.

down the roof of the mouth and also causing slight proptosis on the left side. Periosteal elevation in leukæmia is generally due to leukæmic infiltration underneath the periosteum (Forkner, 1938). Such changes have been described in both myeloid and lymphatic leukæmia. There is no reference to bony lesions in acute monocytic leukæmia in Forkner's monograph (Forkner, 1938). Recently, Freeman and Koletsky (1939) have reported destructive lesions of bone, especially in the hands, in a case of chronic monocytic leukæmia.

The diagnosis in all the cases was based on hæmatological findings, a summary of which has been given in table VI. The criteria of hæmatological diagnosis of acute monocytic leukæmia are:— (i) the predominant leucocytes are of a uniform type and are immature, *viz*, monoblasts and premonocytes, (ii) increase of total leucocyte count, though often not a great increase, (iii) rapid and progressive anæmia, and (iv) in the sternal marrow hyperplasia and leucoblastic reaction with marked preponderance of monoblasts and premonocytes, and in general a great

the blood picture and examination of sternal marrow smears by means of modern hæmatological methods, however, generally enables a differentiation to be made between the different blast cells, and hence makes possible a correct diagnosis of the type of leukæmia. The staining methods that are useful are (i) May-Grünwald-Giemsa staining, (ii) modified Sato and Sekiya method of peroxidase staining, (iii) supravital stain by neutral red and Janus green. The following table (VII) gives the chief differentiating features of the three types of blast cells:—

Histological examination of tissues is of much less help in the diagnosis of the type in acute leukæmia as differentiation between the different blast cells is much more difficult in paraffin sections than in blood or marrow smears. In no case of this series was a histological examination possible. For details as to histological differentiation Forkner's article on the subject may be consulted (Forkner, 1939).

Prognosis and treatment.—The disease is uniformly fatal; Warren (1929) and Forkner

(1938) found that 84 per cent of patients died within two months and practically all within six months. The duration in our three cases which could be followed to the termination was about five months. Blood transfusions, repeated frequently, and the administration of hæmatinics will prolong life to some extent, and these were tried in our cases, in the hope that these measures by prolonging life might turn the disease into the chronic form, but these hopes were not fulfilled. Deep x-ray exposures are apparently quite useless.

Summary

1. Four cases of acute monocytic leukaemia, in Indians, are reported; their clinical and hæmatological features are analysed and the peculiarities noted in some of these cases discussed.

2. The modern methods of hæmatological diagnosis of this type of acute leukaemia are described.

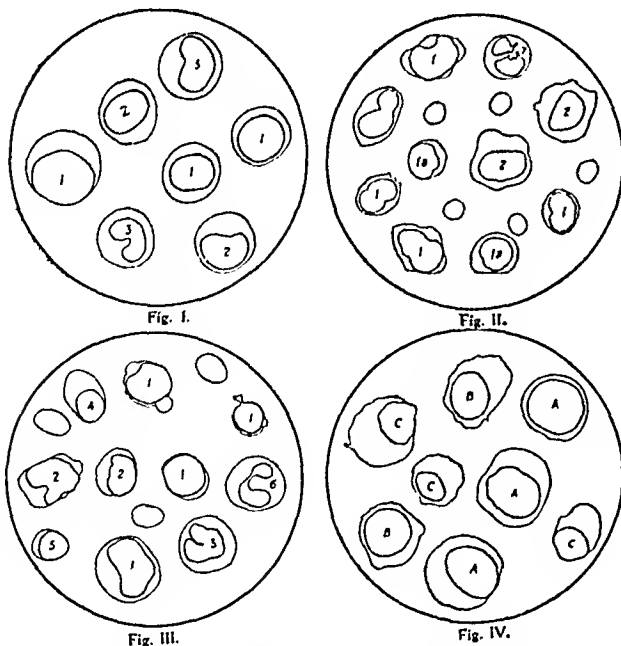
3. Some evidence has been set forth which appears to suggest a close relationship between Hodgkin's disease and monocytic leukaemia.

Acknowledgment

We are thankful to Dr. R. N. Chaudhuri for the clinical notes of case II. Our thanks are due to Professor G. Hadfield for examining the smears of cases II and III and confirming the identity of the predominant monoblasts.

(Concluded at foot of next column)

KEY TO PLATE I



Acute monocytic leukaemia (figures i, ii and iii)

1. Monoblast. 1a. Monoblast with Auer's body. 2. Premonocyte. 3. Monocyte. 4. Plasma cell. 5. Lymphocyte. 6. Eosinophil. 7. Neutrophil.

Agranulocytosis (figure iv)

A. Plasmablast. B. Preplasmacyte (Türk cell). C. Plasma cell.

AGRANULOCYTOSIS IN KALA-AZAR

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ACUTE agranulocytosis as a complication of kala-azar was first reported by Zia and Forkner (1934) in China. Later, Huang (1940) described 42 cases (including the cases of Zia and Forkner) occurring in a period of ten years during which there were 554 proved cases of kala-azar admitted into the hospital of the Peiping Union Medical College, thus this complication occurred in 7.6 per cent of this series of cases.

In 20 of these 42 cases agranulocytosis was apparently the result of kala-azar *per se* and in 17 it followed the intravenous administration of pentavalent antimonials (neostibosan and urea stibamine); in the rest the cause was undetermined. In India, no authentic case of agranulocytic angina as a complication of kala-azar has been reported hitherto, though since 1934 when Dr. L. E. Napier saw Forkner's cases in China, he and other workers at the Calcutta School of Tropical Medicine have been on the look out for this condition, but no such case was encountered in the several thousands of cases of kala-azar diagnosed and treated during these years. This goes to show the extreme rarity of this complication in kala-azar in India. The case reported below is thus, in all probability, the first reported case of the agranulocytic angina syndrome complicating kala-azar in India.

The patient S, Hindu female, aged 11 years, came to the kala-azar clinic of the Calcutta School of Tropical Medicine on the 17th September, 1942, complaining of fever for four months and inability to swallow anything for the previous four days. The fever commenced as an attack of remittent pyrexia four months before. The irregular type of fever continued and at the time of attending the clinic she showed a low remittent fever. The fever had been unaffected by quinine. During all these months there had not been much impairment of appetite, and digestion had been fair. For the few days preceding, the patient had been

(Continued from previous column)

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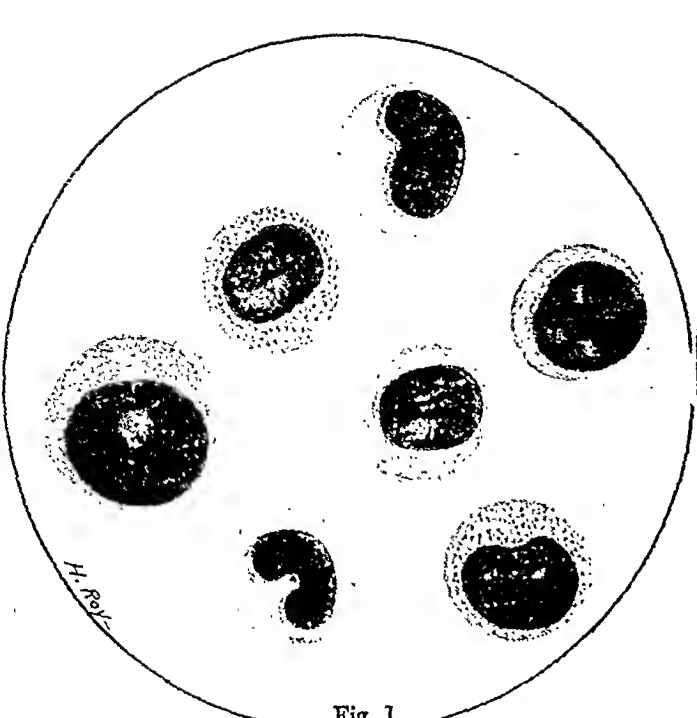


Fig. I.
Monocytic leukæmia.
Case I.

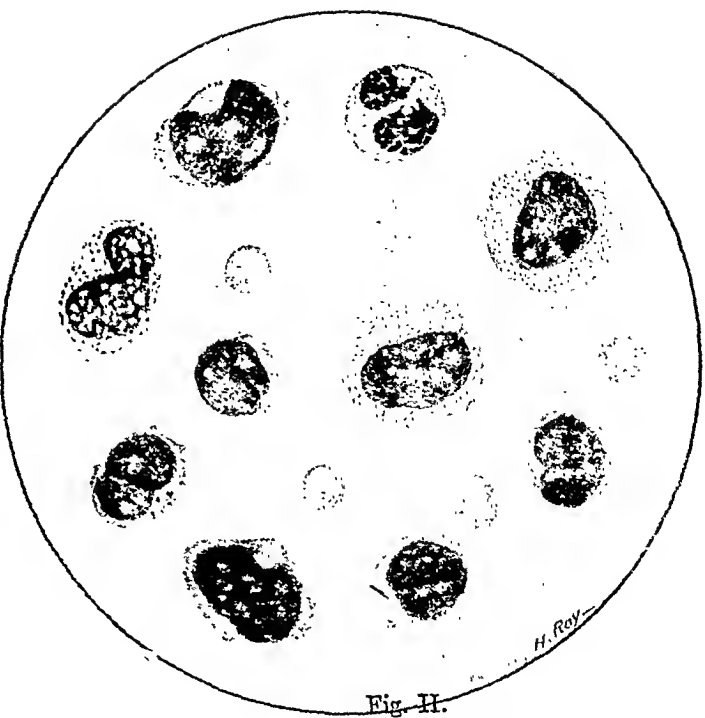


Fig. II.
Monocytic leukæmia.
Case II.

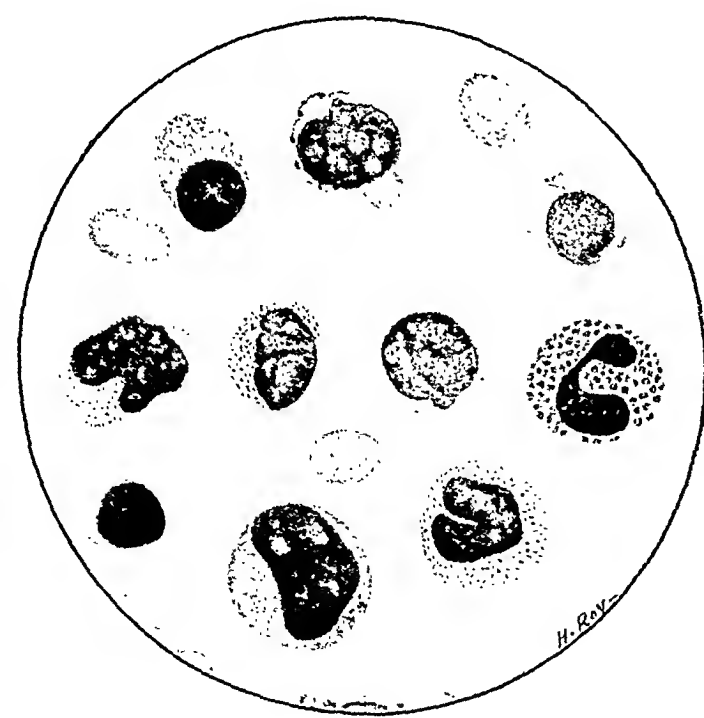


Fig. III.
Monocytic leukæmia.
Case III.

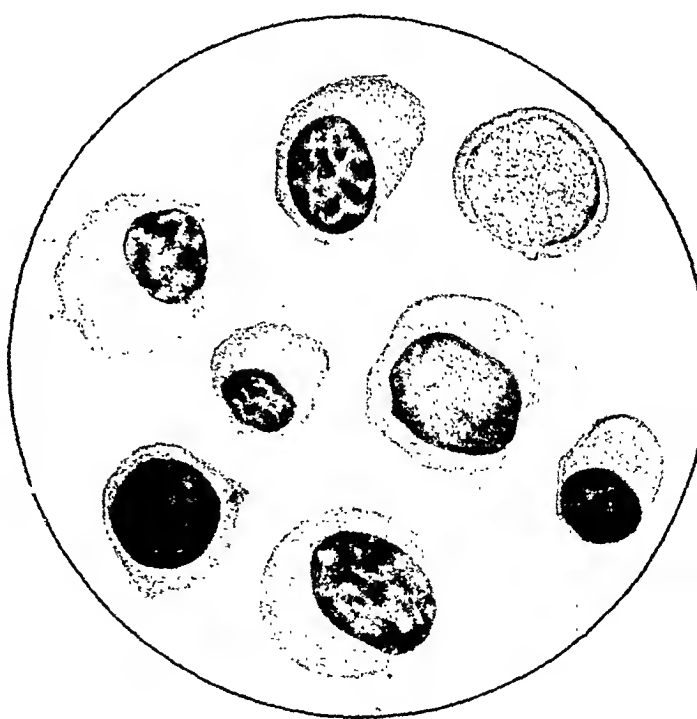


Fig. IV.
Agranulocytosis in kala-azar. Composite
picture of cells from sternal biopsy smear.



Fig. 1.



Fig. 2.



Fig. 3.

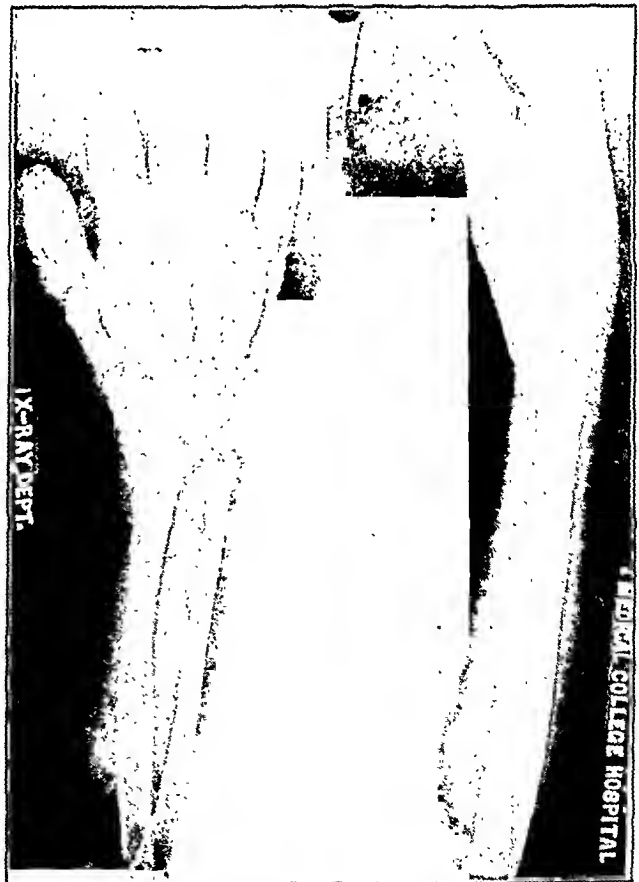


Fig. 4.

having diarrhoea. She was complaining of pain in her throat and was unable to swallow.

The patient had had no treatment for kala-azar. On examination, the patient was found to be emaciated and fairly anæmic. The tongue was coated with a yellowish white fur and was sore at the margins; the pharynx and the tonsils looked congested, but no membrane or pus points were seen. The patient could not swallow the saliva and there was viscid yellowish mucus and saliva in her mouth which she could spit out only with very great difficulty. The cervical lymph glands were enlarged. The heart rate was very rapid, the size and the sounds were normal. The lungs showed evidence of generalized catarrh, and there were medium and fine crepitant râles over the bases, suggestive of broncho-pneumonic areas. The liver was enlarged 1 inch below the costal margin and the spleen too 1 inch below the tip of the ninth left costal cartilage. No other abnormality was detected.

The aldehyde test was found to be positive. As the condition in the mouth and throat suggested agranulocytic angina, a total and differential leucocyte count was done at once. Blood count: white blood cells—750 per c.mm., neutrophils—nil, lymphocytes—600, plasma cells 7.5, preplasmacytes (Türk cells) 60, and large mononuclears 82.5 per c.mm. This confirmed the diagnosis of agranulocytosis.

The patient was admitted the same afternoon in the hospital of the Calcutta School of Tropical Medicine. She looked rather ill and her temperature was 100.4°F., pulse/resp.—144/36. A sternal puncture was done. *Leishmania donovani* was found in fair numbers in the smear. (For report of the myelogram *vide infra*.)

The patient was given an injection of pentnucleotide 5 c.cm. intramuscularly and 25 per cent solution of glucose 25 c.cm. intravenously and fluids were administered per rectum. The oral condition was treated with cleansing with hydrogen peroxide and painting of lotio optochin.

That evening the patient was unable to swallow more than a few teaspoonsful of milk. All night she was very restless and there was difficulty in breathing. The temperature rose to 101.4°F., the pulse was soft and very rapid (? 160/min.) and the respiration 44 per minute. The patient also had several loose stools in the night. She was given an injection of camphor in oil and oxygen inhalations continuously through a nasal catheter.

In the morning the patient was semi-conscious and the dyspnoea had increased, the pulse was barely palpable (? 164/min.). The general condition rapidly grew worse, and the patient died at 9 a.m. on 18th September, 1942.

Laboratory investigations.—Culture of swab from the tongue—heavy growth of monilia.

Report of sternal puncture

Total nucleated cells	..	16,000 per c.mm.
Differential count—		
Endothelial cells	..	2.25 per cent.
Megaloblast	..	0.50 " "
Erythroblast	..	nil
Normoblast	..	9.75 " "
Myeloblast	..	0.25 " "
Premyelocyte	..	1.75 " "
Neutrophil myelocyte	..	8.50 " "
" metamyelocyte	..	nil
" band forms	..	0.5 " "
" segmented	..	nil
Eosinophil	..	nil
Basophil	..	0.25 " "
Lymphoblast	..	nil
Lymphocyte	..	46.25 " "
Plasmablast	..	6.0 " "
Preplasmacyte	..	7.25 " "
Plasma cell	..	11.25 " "
Monoblast	..	nil
Premonocyte	..	0.75 " "
Monocyte	..	3.25 " "
Megakaryocyte	..	0.75 " "

Mitotic cells +, *Leishmania donovani* +

Note on the unusual cells found in the sternal-marrow smear

In describing the cells of the plasmacyte series, Osgood and Ashworth (1937) denote the stem cell as the plasmablasts, the next stage as the preplasmacytes or Türk cell, and the fully mature cell as the plasma cell.

In the smears made from material obtained by sternal puncture, all the three cells of the plasmacyte series were found in quite appreciable numbers; they formed about 25 per cent of the total nucleated cells. (See plate I, fig. IV.)

The stem cells or plasmablasts seen in the stained smears were big cells with sizes varying from 11 to 24 microns. They were round or oval in shape with irregular cell outlines. The cytoplasm was opaque and stained a dirty deep blue colour with May-Grünwald and Giemsa staining. In most of the cells there was a number of small vacuoles in the cytoplasm.

The nucleus was round or oval in shape and occupied more than two-thirds of the cell. The chromatin structure of the nucleus was very fine. In many of the cells a few ill-defined nucleoli could be seen. There was no condensation of the nucleus at the periphery.

The cells described above closely resemble megaloblasts. There is hardly any difference in the chromatin structure of the two cells. But though the cytoplasm is opaque in both, the colour (of the cytoplasm) is distinctive in the two cells. While the colour of the cytoplasm of plasmablasts is dirty blue, the colour of the cytoplasm of megaloblasts is dirty grey. The clear open space or 'halo' round the nucleus which is often seen in the megaloblasts is seldom noticed in plasmablasts.

The distinction of these cells from myeloblasts was comparatively easy in most cases. The absence of characteristic nucleoli and the opacity and coloration of the cytoplasm were the main features by which these cells were differentiated from the more commonly found myeloblasts.

Though megaloblasts are the cells which are more frequently found in a sternal puncture smear of a case of anæmia, the cells described above were identified as plasmablasts and differentiated from megaloblasts on the characteristics mentioned above and also on account of the preponderance of the cells of the plasmacyte series in the smears for a 'cell is known by the company it keeps'. For the same reason a few of the atypical blast cells may have been included as plasmablasts.

Comment on the Bone-Marrow Findings

Bone-marrow in agranulocytosis.—The condition of the bone-marrow in agranulocytosis has been very fully described by many workers, amongst whom mention may be made of Fitz-Hugh and Krumbhaar (1932); Fitz-Hugh and Comroe (1933); Jaffé (1933); Custer (1935); Darling, Parker and Jackson (1936) and Schattenberg (1937). All these workers are unanimous in their opinion that with rare

exceptions the marrow in agranulocytosis is normal or hyperplastic and that there is no obvious change in the red-cell series. But the workers differ in their findings of the different types of leucocytes in the marrow. Fitz-Hugh and Krumbhaar and later Fitz-Hugh and Comroe found an increase of myeloblasts in the marrow and suggested that this was due to 'maturation arrest' of the myeloblasts, in the same way as there was maturation arrest of megaloblasts in cases of pernicious anæmia, and that agranulocytosis is a disease entity. These workers are supported by Custer, Darling *et al.* and Schattenburgh. But a discordant note is sounded by Jaffé who suggests that agranulocytosis is not a disease entity but a symptom-complex and can be caused by any toxic or infectious agent. This worker reported great increase of lymphocytes and plasma cells. The increase in the plasma cells is also reported by Darling *et al.* in those cases in which death took place after about two weeks or more.

Bone-marrow in kala-azar.—The mean values of the sternum puncture findings in 29 cases of kala-azar (Napier, 1938) are given in the table below together with the normal findings in Indians. It will be seen that, though the total nucleated-cell count is about the same in both, the proportion of white blood cells is definitely lower in the kala-azar cases, due to decrease of the granulocytes, and there is proportionate increase of the red-cell series. It will also be seen that there is a definite increase of plasma cells in the kala-azar cases, these being more than 3 per cent of the total nucleated cells, as against 0.6 per cent in the normals.

Mean values of sternal puncture findings

	In normal population	In kala-azar
Total nucleated cells ..	53,500	58,000
Differential count—		
Endothelial cells
Megaloblast ..	0.7	1.6
Erythroblast ..	3.4	2.05
Normoblast ..	21.6	36.31
Myeloblast ..	1.2	0.90
Premyelocyte ..	0.7	1.09
Neutrophil myelocyte ..	4.4	7.86
" metamyelocyte ..	9.7	8.79
" band forms ..	25.3	22.5
" segmented ..	16.8	3.75
" ..	1.3	0.63
Eosinophil ..	4.7	1.52
Basophil ..	0.2	0.1
Lymphoblast
Lymphocyte ..	6.25	6.16
Plasmablast
Preplasmacyte
Plasma cell ..	0.6	3.04
Monoblast
Premonocyte
Monocyte ..	3.0	2.90
Megakaryocyte

Bone-marrow in agranulocytosis in kala-azar.—Agranulocytosis occurring in cases of kala-azar was found to be prevalent only in China by Zia and Forkner (1934) and later

by Huang (1940), but the study of the bone-marrow was not done in either series.

In the reported case, our findings in the bone-marrow obtained by sternal biopsy differ markedly from the usual findings as reported above mainly in the following points:—

1. The marrow was neither normal nor hyperplastic, but appeared to be definitely hypoplastic, since the total nucleated cell count was only 16,000 per c.mm.

2. The increase in lymphocyte and plasma-cell series is more than is found in either of the above diseases.

3. In addition to the reduction of granulocytes, there was also a reduction of erythropoietic cells which is not generally found in either kala-azar or agranulocytosis.

It is very hard to explain these marked differences in the bone-marrow findings, except as due to two factors, agranulocytosis superimposed on kala-azar. It may not be unreasonable to suppose that on account of well-developed kala-azar in this case, the marrow had a tendency towards decrease of cells of the granulocyte series and increase of plasmacytes. The super-imposition of the pathological factor that causes agranulocytosis, which is sometimes accompanied by increase in plasma cells, was probably responsible for the production of extreme granulopenia and the relative plasmacytosis in a marrow which was already granulopenic and slightly plasmacytic in reaction. The presence of plasmablasts, though very unusual, is not difficult to explain, for the excess of the cells of plasmacyte series, both in the blood and in the marrow, was certainly due to rapid formation of these cells in an otherwise hypoplastic marrow. With such rapid formation, maturation of the cells could not be expected to take place in the usual way, the result being the presence of a number of Türk cells in the blood and both Türk cells and plasmablasts in the marrow.

Conclusion.—The diagnosis of agranulocytic angina in this case was based on (i) soreness of the mouth and throat with inability to swallow, (ii) peripheral blood showing a complete absence of granulocytes, (iii) sternal-marrow biopsy showing hypoplastic marrow with extreme paucity of cells of the granulocyte series, and also of the red-cell series. The preponderating element in the smear was made up by lymphocytes, plasma cells and the precursors of the plasma cells. That it was a case of kala-azar was evident from the presence of *Leishmania donovani* in the sternal-marrow smear and from the positive aldehyde test.

The condition of agranulocytosis was probably not due to kala-azar alone but to the superimposition of some factor causing agranulocytosis in an untreated case of kala-azar.

Summary.—A case of kala-azar with the agranulocytic angina syndrome is described. This is the first authentic case reported in India.

(Concluded on next page)

COLIFORM-GROUP INFECTIONS OF THE URINARY TRACT: THEIR CLINICAL TYPES AND INCIDENCE IN MYSORE

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SURVEYING the usual causes of fever among the hospitalized patients in medical wards in this country, we find, in order of frequency, malaria, pneumonia, enteric fever, hepatitis and liver abscess; acute bacillary and malarial dysentery, rheumatic fever with or without carditis and typhus are found comparatively rarely in Mysore. Apart from these well-known febrile diseases we find a large group of fever cases under several vague headings such as enteric or paratyphoid without a diagnostic Widal, chronic tonsillitis and sinusitis, where the ear-nose-throat specialist has to press very hard to satisfy the physician, and the host of septicæmias of doubtful origin, from pyorrhœa alveolaris to the unfortunate appendix which does not empty its contents speedily enough. It should not be denied that cases of oral sepsis occur among our patients; Dr. B. K. Ramakrishna Rao and one of us (H.) have demonstrated an elderly man who was saved from death from a severe

(Continued from previous page)

Acute agranulocytosis with angina is an exceedingly rare complication of kala-azar in India.

The sternal marrow biopsy showed an hypoplastic condition. The cytological picture in this case and the unusual cells encountered are described.

Acknowledgment.—Our thanks are due to Dr. L. E. Napier, under whom the patient was admitted, for kindly allowing us to report this case.

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toxæmia with high fever and incessant hiccough, by the extraction of three teeth bearing root abscesses, and it is certainly better to remove five appendices unnecessarily than to overlook one which needed operation. But still, after excluding all these recognized ætiological factors, we have to face the extremely unsatisfying diagnosis 'F. U. O.' (fever of unknown origin) in a varying but fairly high percentage of our patients—unless we examine microscopically the urine sediment of at least all those cases which are not convincingly diagnosed. Surprisingly frequently red blood cells and leucocytes are found in the catheter urine of patients who have never complained of any urinary tract disturbances, such as burning sensation when passing urine, frequency of micturition, nocturia or any pain referable to the kidneys or the bladder; such findings may be made in the urine of patients who do not show even traces of albumin in the urine.

Starting from this fact that many patients, with otherwise inexplicable fever or constitutional disturbances, show a pyuria and/or a microscopic hæmaturia, we pursued several lines of investigation to answer the following questions:—

(1) What clinical signs and symptoms are so regularly associated with signs of urinary tract infection that we may safely assume a causal connection between them; or to put it the other way round: what are the clinical conditions in which we have to search carefully and repeatedly for a coliform group infection as the ætiological factor?

(2) How do the signs of general infection or toxæmia, which are present along with objective findings of a urinary-tract infection, respond to the treatment with urinary disinfectants?

Do we find a strict parallelism between general improvement and urinary findings? What is the prognosis of these cases?

(3) How frequently are urinary-tract infections to be found among our hospital patients? Which are the causative organisms?

(4) Do the leucocyte count and the sedimentation rate help in the differential diagnosis?

The specimens of urine have been collected under strictly aseptic conditions; for the examination of urine of females, only catheter specimens were used; catheterization was performed by two specially trained, reliable nurses.

The answer to the first question is contained in a description of the way we proceeded actually to find the correct diagnosis in several groups of patients, where the findings, apart from those in the urine, did not suffice to explain the clinical picture. The majority of these cases showed fever of widely varying type as the only objective sign; in almost all of our patients some definite proof of a malarial infection is present; either the parasites are found or the flocculation test is positive or the spleen is enlarged—but it is frequently very difficult to decide whether the fever of an individual case is really due to malaria. If a course of five days'

TABLE

MEN													
Month	Admissions	Infected cases		TEMPERATURE					TREATMENT				
		Total	%	Afebrile	Febrile				Hexamine I-V	Sulfo. group	Hexam. + sulfo.	Mixt.	Untreated
					Low	Irregular	High interm.	High contin.					
1941 III	112	1	1	Ps 1	1
IV	110	1	1	O 1	1
V	115	6	5.	..	A 1	..	C 1 Ps 1 O 1	A 1 O 1	4	1	1
VI	126	6	5	C 3 O 1	A 1	A 1	3	..	3
VII	119	5	4	C 2	C 1 A 1	C-A 1	1	2	2
VIII	104	3	3	..	C 2	..	C 1	..	1	1	1
IX	99	6	6	C 1	C 1	C 2 A 1	C 1	..	5	1
X	107	7	6.5	C 3	C 1	C 2 P 1	3	4
XI	107	2	2	C 1	O 1	1	1
XII	116	5	4	C 2	C-A 1 A 1	C 1	2	..	Pyelop + Mandecal	..	2
1942 I	134	14	10.4	C 4 A 2	C 1 Ps 1	C 3	C 2 A 1	..	8	1	1	1	4
TOTAL	1,246	56	4.5	15	12	16	10	3	28	3	6	4	15
				26.8%	21.4%	28.5%	18%	5.3%	50%	5.3%	10.6%	7.4%	26.7%

Abbreviations :

C 1 = *Escherichia coli* 1 case.
 A 2 = *Aerobacter aerog.* 2 cases.
 P 1 = *Proteus vulgaris* 1 case.
 Ps 1 = *Pseudomonas* 1 case.

I

WOMEN

Admission	Infected cases		TEMPERATURE					TREATMENT				
			Afebrile	Febrile				Hexamine I-V	Sulfo. group	Hexam. + sulfo.	Mixt.	Untreated
	Total	%		Low	Irregular	High interm.	High contin.					
58	10	17	A 1	C 2 C-A 1	C 2	C-Ps 1	C 3	9	1
50	9	18	C 2	..	C + C 1 A 1 C-A 1	C + C 1	C-A 1	3	..	1 Hexam. + maphars	2	2
61	12	20	..	C 2	C 4 C-P 1	C +	C-A + C-A 1 O 2	9	..	3
52	12	23	C 2	C 1 A 2	C 1	C 2 A 1	C 2 O 1	4	..	4	1	3
55	20	36	C 1 P-A 1	C 5 C-A 2 C-Ps 1 P 1	C - C 6 A 1	..	C-A 1	11	1	2	4	2
51	15	30	A 1 P-A 1	C + C 9	C 2 C-A 1	9	..	1 Pyelop + Mandecal	2	2
42	16	38	C-8 C-A 1	C + C-A 1 A 1	C 3 A 1	7	1	..	1	7
50	21	42	C 5 Ps 1	C 2 A 4	C 6 A 1	C 2	..	12	2	7
44	5	11	C 1	C 2	C 1 C-P 1	2	..	2	..	1
43	5	11	C 2	C 2	C 1	3	2
58	12	20.7	C 1	C 4	C 3	C + A 1 Ps 1 O 1	..	6	2	1	..	12
564	137	24.3	28 20.4%	44 32%	40 30%	13 9.4%	12 8.2%	75 54.7%	6 4.3%	14 10% other comb. 2 2%	10 7%	30 2%
			Mortality	2 4.4%	2 4.8%	3 23%	1 8.3%					

C-A + = *E. coli* and *Errobacter* 1 fatal case.C-P 1 = *E. coli* and *proteus* 1 case.C-Ps 1 = *E. coli* and *psudomonas* 1 case.P-A 1 = *Proteus* and *Errobacter* 1 case.

O 1 = Culture sterile 1 case.

quinine treatment does not influence the character of the fever curve, we can safely exclude malaria as the cause of the raised temperature. Lung conditions are comparatively easily diagnosed, though not always from the physical findings alone; but if neither the clinical nor the x-ray examination show a focus in the lungs and there is no pathological sputum, we are compelled to search for another cause of the fever. If we can exclude the acute and chronic dysenteries, ulcerous colitis, hepatitis and liver abscess, enteric and typhus, tonsils, sinuses, the middle ear, the rare cases of oral sepsis from root abscesses, endocarditis and the very rare subacute bacterial endocarditis, chronic inflammations of gall-bladder or appendix, inflammation and abscess of the prostate gland, and gynaecological conditions, which of course is possible only to a certain degree of probability and by no means with the certainty of a chemical experiment, then we think of making pathological findings in the urinary tract responsible for an otherwise inexplicable fever. That does not mean that in practice we wait till all these other possibilities are excluded; before a microscopic examination of the urine sediment and a bacteriological examination by urine culture is performed. But we are not satisfied that the leucocytes and/or red blood cells in the sediment and *Escherichia coli*, grown in the culture, indicate the cause of the fever in the case under investigation unless we have excluded by examinations and, if possible, by therapeutic tests the other possible ætiological factors. Using this method of case analysis, we find a large number of cases, six times more frequently among women than among men, in which the coliform-group infection, proved by pyuria, frequently accompanied by microscopic hæmaturia and, in more than 95 per cent of these cases, by a positive urine culture, is the most probable cause of the actual febrile condition.

The chart shows that low fevers, irregular fever curves with afebrile periods alternating with two or three days of a temperature reaching 101° and more, high intermittent fever, imitating malaria, and high continuous fever are to be found among the urinary tract infections. 73 per cent of the male and 79.6 per cent of the female patients, in whom a coliform-group infection was found, suffer from fever of one of these types. The similarity in the distribution of afebrile and febrile cases among men and women, in spite of the great difference in the total incidence, is striking. Among the cases with high intermittent fever were two young women, admitted in a violently delirious condition of deep unconsciousness, closely resembling cases of cerebral malaria; as no other signs of malaria were found, but those of a urinary infection were definitely present, a course of pyelopurin injections was started; after two or three of them, the fever subsided and a perfectly normal mental condition was restored; though the cerebrospinal fluid was not examined, these

are most probably some of the rarely occurring coli-meningitis cases.

Another important though not very large group is represented by certain anæmias. In most of our cases of severe hypochromic anæmia which are admitted with a hæmoglobin content of 10 to 15 per cent (Sahli) and a colour index of about 0.5, hookworm ova are found in the fæces. An uncomplicated hookworm anæmia improves quickly when iron is supplied in sufficient doses*. This favourable response is regularly elicited, without previous deworming and independent of the heaviness of worm-infestation [Napier (1937), Napier and Das Gupta (1937), Napier, Das Gupta and Majumdar (1941), Payne and Payne (1940), Heilig (1941)]. If the hookworm anæmia does not improve substantially by at least 10 to 15 per cent (Sahli) after a fortnight of the medication with massive doses of iron, we find as a rule that another cause co-exists with the ankylostomiasis which prevents the improvement of the blood condition; here again we have to search carefully for a urinary-tract infection which is in our experience one of the common anæmia-maintaining factors. The coliform-group infection manifests itself in these cases sometimes by short periods of a slightly or moderately raised temperature; but other patients of the same group are entirely afebrile for weeks of observation, and nothing but the microscopic and bacteriological examination of urine will reveal the cause of the poor response to an otherwise surprisingly effective treatment. It is of the greatest importance to detect these cases, as no anti-anæmic treatment whatever is effective in these patients, unless the coliform-group infection is properly treated.

Apart from fever and these dangerous hypochromic anæmias which are caused or complicated by *E. coli*, the symptoms of subacute or chronic arthritis and the vague complaints of weakness, lassitude, loss of appetite, etc., are sometimes caused by urinary-tract infections. We do not attempt to present a general solution for all the diagnostic difficulties which we have to face in these patients with more than one infection; on the contrary we advise against the over-estimation of the importance of a few pus cells in the urine, or a few *E. coli* colonies in the culture; but we also emphasize the danger of overlooking the possibility of such an infection, a mistake easily committed in the absence of albuminuria or of local complaints referable to the urinary tract.

The therapeutic response is summarized in the chart under the heading 'treatment'; in fact the therapeutic test is one of the most important and reliable corroborations of the diagnostic assumption that a coliform-group infection is not only present in the given case but also responsible for the pathological signs referred to

* Our routine medication is the administration of freshly prepared Bland's pills, gr. 90 per day.

it. If a continuous fever which lasts for weeks in spite of the most concentrated antimalarial treatment (as has happened in several of our cases treated outside the hospital) disappears completely and lastingly after a few intravenous injections of 20 to 30 grains of hexamine, we certainly are justified in assuming a urinary-tract infection, proved to be present by objective findings, as the cause of the fever. If a hypochromic anæmia (in our material mostly to be found in hookworm disease) does not respond to any anti-anæmic treatment unless a complicating coli infection is brought under control, one is entitled to say that this infection was responsible for the poor response or for the deterioration of the anæmic condition. The figures show that 50 per cent of such patients respond satisfactorily—in the sense just described—to intravenous hexamine injection prepared in the hospital, or to pyelopurin; if five of these injections did not stop the fever completely, we usually tried a sulphonamide or sulphapyridine preparation, which we found effective in 4.3 per cent of the female and in 5.3 per cent of the male patients; however in about 10 per cent of men and women equally, we had to use a combined medication of intravenous pyelopurin and M.&B. 693 prontosil or sulphanilamide orally to bring the fever under control. In the cases of refractory anæmia with joint and body pains and complaints of vague disturbances, hexamine was injected. In 27 per cent of our cases, a (mostly mild) urinary-tract infection was present, but remained untreated; this percentage is exactly the same as that of our afebrile cases. That means that the fever or the constitutional disturbances of these patients responded well to some other treatment, such as quinine, emetine, or salicylates, so that the coliform group was not held responsible for the pathological signs. Equally such cases of pneumonia combined with urinary-tract infection as became and remained afebrile after 24 to 36 hours of sulphapyridine medication were classified as 'afebrile' and 'untreated' so far as the coliform-group infection is concerned, though we admit that by strictly applying this method some cases might have been placed wrongly in the afebrile group.

The therapeutic effect of these urinary disinfectants on fever, iron-refractory anæmias and some of the general complaints mentioned before is so reliable that the diagnosis may be almost based on and checked by it. In the vast majority of these cases the microscopic and bacteriological urinary findings improve accordingly, though more slowly—just as in pneumonias under sulphapyridine treatment fever and signs of toxæmia subside much sooner than the physical signs. In those cases in which intravenous hexamine injections do not remedy the microscopic deposit or sterilize the urine, a six days' course of sulphanilamide, one tablet thrice a day, is indicated and succeeds almost always in sterilizing the urinary tract. Our experience

with sulphathiazole is very limited but highly encouraging.

The prognosis of the coliform-group infection proper is good; we lost no male and only three female patients, or 2 per cent, due to this infection, two of them showing high intermittent fever with *E. coli* growing in the culture, and one showing high continuous fever with a combined growth of *E. coli* and *aerobacter*; the remaining five deaths making a total mortality of 5.8 per cent (among women) occurred in badly emaciated females admitted to the hospital in the terminal stage of chronic diarrhoea. However, the prognosis is very good in men and in the afebrile cases in women amongst whom there was no mortality. The prognosis becomes worse from the low febrile cases in females with a 4.4 per cent death rate, to the irregular fevers with 4.8 per cent, to the continuous fevers with 8 per cent mortality, and is by far the worst among women with septic or high intermittent fever, of whom 23 per cent died. Each of those percentage figures is calculated from the corresponding fever group, not from the total number of infected cases.

The frequency shown in the chart is rather too low than too high because during the eleven months from March 1941 to January 1942 only those cases have been examined for a urinary-tract infection in which such an infection was suspected on clinical grounds. And yet 4.5 per cent of 1,246 men admitted to the medical unit during this period, and 24.3 per cent of 564 women, had coliform-group infections proved by positive findings in the urine sediment, and confirmed in all but nine cases by at least one positive urine culture. It is interesting to note the sharp decline in the number of infected females during November and December; but only the experience of several years will decide whether a typical seasonal incidence really exists. To check the reliability of our figures we calculated first the total number of infections, the percentage from the total of admissions, the distribution per cent of the different clinical types, the therapeutic response to the various drugs used, and the mortality for the ten months from March to December; then all these figures were recalculated after adding the results for January; the difference was nowhere more than 0.3 per cent in the larger figures and reached 5 per cent only in the smallest groups; all the other percentage figures remained practically unchanged, proving that our material is large enough to yield reliable information.

We used also another method to find out whether our figures represent the real incidence of urinary-tract infections or whether a certain amount remains undetected. The urine of all the female patients admitted to the medical wards during February 1942 was examined microscopically and bacteriologically; among sixty admissions, eighteen, 30 per cent, had coliform-group infections; the average incidence for four months (from July to October it was 30

per cent) was 42 per cent. This comparison makes it very probable that most of the infections are detected when a detailed urine examination is performed only in clinically suspicious cases.

prove of some value in the differentiation of active and inactive urinary-tract infections, and in deciding whether the fever is due to the urinary infection or to another co-existent pathological condition. This expectation was

TABLE II
Abbreviations as in table I

MEN			WOMEN		
Organism	INFECTED CASES		Organism	INFECTED CASES	
	Total	%		Total	%
C	35	62.5	C	98	71.5
A	10	18	A	15	10.7
P	1	1.5	P	1	0.7
Ps	3	6	Ps	2	1.5
C-A	2	3	C-A	11	8.2
C-P	C-P	2	1.5
P-A	P-A	2	1.5
			C-Ps	2	1.5
O	5	9	O	4	2.9
..	56	100	..	137	100

Bacteriological examinations gave the following results : 62.5 per cent of the male cases and 71.5 per cent of the female patients were infected with *E. coli* only, 21 per cent and 20.1 per cent respectively with *Aerobacter aerogenes* alone or combined with *E. coli* or proteus; the rest were due to mixed infections as shown in table II and a few cases to proteus or pseudomonas only; taking all the cases together in which *E. coli* was found at all, it is present in 66 per cent of the men and 84 per cent of the women who harbour urinary-tract infections.

Leucocyte counts have been made in 82 of these cases; in conformity with previous investigations we may say that the coliform group does not influence the white blood picture in a characteristic way. Forty-eight of these leucocyte counts show figures between 5,000 and 10,000, ten slightly below 5,000 and only twenty-four show a moderate leucocytosis up to 15,000; or, in other words, two-thirds have leucocyte counts within normal limits; in the remaining third it is almost always possible to trace the cause of the leucocytosis to another infection co-existent with the coliform group. This result makes it possible to state with a probability of at least 2:1 that a case of a coliform-group infection showing a leucocytosis is complicated with some other factor responsible for the increased leucocyte count.

Sedimentation rate.—We expected that the sedimentation velocity of the erythrocytes would

not fulfilled; the range of the sedimentation velocity found in our cases is too great to permit any definite conclusion at present.

Discussion

To survey the enormous literature on urinary-tract infections and the importance of the coliform group in the causation of pathological processes manifested, apart from kidney and bladder, in liver, joints, nervous system, etc., is neither intended nor possible in the present circumstances; especially the French contributions to the understanding of the complicated and ever-changing clinical pictures of coli-infections are not available in detail; they are summarized by Desgorges (1932). The great difficulty and even impossibility of diagnosing a urinary-tract infection from the patient's history and complaints is not sufficiently emphasized in many of the recent textbooks; the symptomatology, never found among our patients, characterized by frequency of and burning sensation during or after micturition, pain in the bladder, the suprapubic or lumbar region, is still put forward as a regular occurrence (Walker, 1936; Morson, 1937); the absence of bladder symptoms is recognized only for coli-septicemias (Manson-Bahr, 1940). Experiences in full accord with ours, reported above, have been published recently by Marple (1941); he found that complaints pointing to the urinary tract were more frequent among women with a urine normal

on microscopic and bacteriological examination than among those with a urinary-tract infection. The same author investigated the frequency of urinary infections in an unselected group of one hundred women; he found a positive urine culture in 31 per cent of them; taking into account the small number of his cases and the very different external conditions (in California) this result is surprisingly similar to that found in Mysore, with 24.3 per cent infections among 564 women who have been examined for a urinary infection only when its presence was suspected on clinical grounds. It is identical with the infection rate of 30 per cent which we found when all female admissions were examined during the month of February.

The incidence of 30 per cent infected cases found by examining every case during one month and that of 24.3 per cent in the average of eleven months makes it very probable that, even by examining on clinical suspicion alone, hardly any urinary infections are overlooked. The infection rate of women in this hospital is six times higher than that of men; European and American literature shows a ratio of 3 to 4 women: 1 man. These figures show clearly that the female urinary tract is far more exposed to infection, which is in our material certainly due to the numerous pregnancies and deliveries under highly unhygienic conditions. The great difference between the number of infected men and women indicates that the intestinal tract is less important than the genital tract as a source of coliform-group infection, though practically every long lasting diarrhoea is accompanied by a urinary coli-infection (Leishman, 1939); but diarrhoeas are almost equally frequent among men and women.

The percentage of afebrile, low and irregularly febrile cases is almost the same among males and females; each of these groups comprises about 20 to 30 per cent of the total. Roughly 20 per cent of either sex show high intermittent or high continuous fever and represent most probably coliform-group septicæmias. Rigor was conspicuously rare, even in this group which has a doubtful prognosis among women; 3 to 23 per cent of the 'high intermittent' and 1 to 8 per cent of the high continuous fever cases in females died; three of those four deaths were apparently due directly to a septicæmia caused by *E. coli*.

Our therapeutic results seem to show that the old method of injecting hexamine intravenously in doses of 20 to 30 grains on consecutive days is a reliable and powerful means of disinfecting the urinary tract (Wright, 1934). There is no doubt that alkaline mixtures, even in very large doses, exercise hardly any sterilizing action. Rehfuß (1931) convincing experiments have shown that *E. coli* grows with the greatest virulence in the strongly alkaline gall-bladder and bile tract. Normal gastric acidity makes experimental coli-infections by mouth impossible. These facts should be sufficient to prevent the

loss of precious time by trying to disinfect the urinary tract with potassium citrate, sodium bicarbonate, etc. The good results which have been obtained with ketogenic diet in man are another proof that *E. coli* thrives better in alkaline than in acid urine. Where intravenous administration of hexamine does not act satisfactorily, either sulphanilamide or sulphapyridine, or a combination of one of these compounds with intravenous hexamine injections, controls practically every coliform-group infection. The causative organisms in our cases have been *E. coli* alone or combined with *A. ærogenes* in 66 per cent of infected men and 84 per cent of infected women; *A. ærogenes* was found in about 20 per cent of these patients. The other members of the coliform group, like pseudomonas and proteus, were responsible for the remaining infections. Strepto- and staphylococcal infections were not found in our cases; whether this fact is due to a secondary overgrowth of *E. coli* (Marple, 1941) cannot be decided. That such an overgrowth did not take place between catheterization and bacteriological examination is certain, as the catheter specimen was put in the medium within 30 minutes. It is possible however that in urinary-tract infections of long standing such a suppression of cocci occurs.

Conclusion

In our hospital patients, urinary-tract infections do not cause any local symptoms. This fact, taken together with the high incidence of such infections, especially in women, makes it necessary to examine the urine microscopically and, whenever possible, bacteriologically in every case of 'fever of known origin', of iron-refractory hypochromic anaemia, chronic diarrhoea and arthritis.

About 75 per cent of these cases are febrile, but there is no characteristic type of fever; low and irregular fevers are seen with almost equal frequency; high continuous and septic intermittent fevers are more rarely found. The correct diagnosis is of the greatest importance because all the pathological symptoms and signs yield easily to urinary disinfectants and no other treatment is of any avail. Alkalinizing treatment should be abandoned as unreliable and hardly ever of lasting effect. The best urinary disinfectants are certainly sulphonamide, sulphapyridine and sulphathiazole preparations (Vose and Rammelkamp, 1941*). Their prohibitive price prevents their use in every case of urinary infection. They have been used only in those cases in which intravenous hexamine injections did not act satisfactorily, which happened, however, only in about 15 per cent of the cases. All the infections were caused by the coliform bacilli; *E. coli* was by far the most common organism found. The general prognosis is good;

* The different opinion of Allen *et al.* (1939) is based on the therapeutic results in only eight cases.

it is least favourable in women with high intermittent fever. This condition is due, most probably, to a coli-septicæmia. The leucocyte count in most of the urinary infections is normal; figures of more than 10,000 are found exceptionally, and mostly in cases where other infections are co-existent.

Summary

The incidence of urinary-tract infections was estimated among 1,246 men and 564 women admitted to the medical wards during a period of eleven months. These patients were examined for urinary infections only when such an infection was suspected on clinical grounds.

During one month all patients admitted to the female ward were examined for urinary infections.

The results are reported, the clinical pictures described and the incidence of afebrile, low, irregular, high intermittent and high continuous fevers is calculated; the absolute and percentage figures are given in a table for men and women separately.

The mortality is calculated for each of the different fever types.

The treatment used in every case is recorded in the table; the total number and percentage of patients treated with the different kinds of remedies are recorded; the respective merits of several lines of treatment are discussed.

The causative organisms are indicated in the table for every month, for men and women separately. The number and percentage of cases due to each of the pathogenic organisms are calculated.

The results of leucocyte counts are reported.

Dr. V. R. Naidu, M.B.C.P. (Lond.), our pathologist, and Dr. A. Vasudeva Rao, his assistant, performed all the bacteriological examinations; our sincerest thanks are due to them.

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OBSERVATIONS ON OXYCEPHALY IN A FAMILY

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and

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OXYCEPHALY is one of a number of deformities of the skull which are somewhat allied to one another in their pathogenesis, although they differ widely in their clinical aspects. In an oxycephalic patient, the upper part of the head attains an unusual height, giving rise to a high forehead which slopes to a pointed vertex like a tower or steeple. Hence such a skull is often called a tower skull or steeple head. The supra-orbital ridges are low and feebly marked, and the hairy scalp begins at a high level. The eyes which are unduly prominent (exophthalmos) are set far apart (hypertelorism and are often divergent. The arch of the hard palate is also high and narrow, and there may be a varying degree of prognathism. Sometimes, this condition may be associated with other congenital abnormalities, such as poly- or syndactyly, mongolism, talipes, malformations of the ear, etc.

The general consensus of opinion about the pathogenesis of oxycephaly is that the deformity is primarily due to premature synostosis of certain sutures of the skull. The actual site of the synostosis determines the ultimate form of the deformity, e.g., synostosis at the coronal and lambdoidal sutures leads to the development of an oxycephalic skull; closure of the sagittal suture to the scaphocephalic form, and the closure of the metopic suture to the trigonocephalic form. As a consequence of this premature union of the sutures, further growth of the cranial cavity is arrested, although the cranial contents continue to grow. As a result the intracranial tension rises very considerably. The brain, being thus restricted, grows vertically instead of laterally and anteroposteriorly, and protrudes through an outlet which is usually the anterior fontanelle. This rise in the intracranial tension gives rise to the development of a further set of deformities, e.g., shallowness of the orbit and consequent protrusion of the eyeball, marked enlargement of the sella turcica, depression of the middle cranial fossa, basilar lordosis, obliteration of the sphenoidal sinuses and narrowing of the optic foramina. This

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PLATE III

OBSERVATIONS ON OXYCEPHALY IN A FAMILY : M. N. DE & I. ELLIAS



Fig. 1.



Fig. 3.



Fig. 2.



Fig. 4.

Description of illustrations

Fig. 1.—Showing 1½ year old child with a typical picture of oxycephaly.

Fig. 2.—Radiological appearance of the skull of the child showing characteristic well-marked digital impressions.

Fig. 3.—Family of oxycephalics. Mother with two sons.

Fig. 4.—Radiological picture of the skull of the mother. The digital impressions have almost disappeared, but the sella turcica still remains very big and wide.

PLATE IV

A NOTE ON OCCUPATIONAL DERMATITIS IN THE JUTE INDUSTRY : M. N. RAO. (PAGE 54)

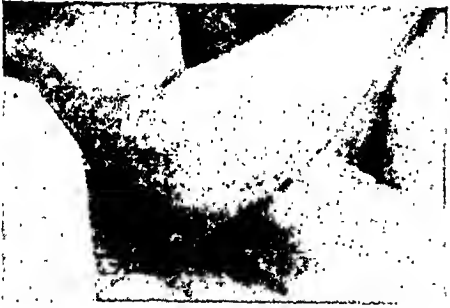


Fig. 1.



Fig. 2.



Fig. 3.



Fig. 4.



Fig. 5.

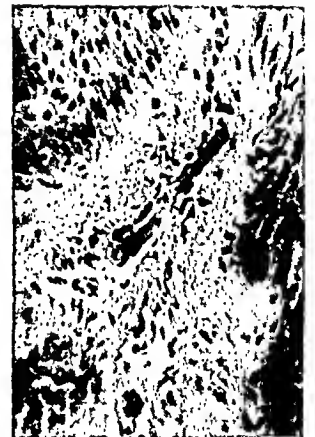


Fig. 6.

Description of illustrations

Fig. 1.—A photograph showing the dermatitis over the postero-lateral aspect of the forearm.

Fig. 2.—A 'contameter' photograph of the same showing the papules at the mouths of the pilo-sebaceous follicles.

Fig. 3.—An unusual site of the dermatitis over the lumbar region.

Fig. 4.—Photomicrograph showing the increase in the layers of the epidermis.

Fig. 5.—Photomicrograph showing the hyperkeratosis.

Fig. 6.—Photomicrograph showing stray round cells and young fibroblasts.

raised intracranial tension is also invoked to explain the digital impressions, best seen in the thinned bones of the vault of the skull in x-ray films.

Oxycephaly usually manifests itself at birth but it may be delayed till the second year of life. Rarely, it may occur as late as the sixth year. In about 10 per cent of cases, the condition has been found to be hereditary or familial. The case which we describe below has a well marked familial character.

Nothing is known regarding the aetiology of the disease and no relationship exists between this and the other commoner diseases which may produce bony deformities such as rickets, syphilis and tuberculosis. It has been suggested that some as yet unknown developmental anomaly may be responsible for it. The hereditary and familial incidence in a certain number of cases and the presence of congenital malformations in others are considered as strong presumptive evidence in support of such a hypothesis.

Oxycephalic children are not necessarily mental cretins, the majority of them showing a fairly normal mental development and functions. A small proportion of these patients may, however, show a state of imbecility. More commonly, they complain of a progressively increasing headache and ultimate loss of vision. The changes in the eyes are very remarkable. In a typical case, one finds exophthalmos, hypertelorism (eyes set far apart), divergent squint, papilloedema and optic atrophy. Exophthalmos, as already mentioned, is due to shallowness of the orbit brought about by the raised intracranial pressure, but the optic atrophy may result primarily from pressure effects due to narrowing of the optic canal or from twisting of the optic nerves due to the development of a deformity of the middle and anterior fossæ of the cranium. It may also follow papilloedema due to heightened intracranial tension.

Oxycephalic children with well marked and characteristic deformity may attain adult age without impairment or loss of vision and without any mental deterioration. Such persons no longer complain of headache. The skulls of such persons are, to all intents and purposes, normal looking, with almost complete disappearance of the digital impressions which form such a characteristic radiological picture. The sella turcica, however, remains very big and widened.

Case report.—N., a male child, aged 1½ years. Admitted into the Medical College Hospital for loss of vision and a prominence in front of the head.

Family history.—The mother has a similar projection in front of her head with protrusion of the eyeballs. Her vision and mental condition are perfectly normal. This deformity in her skull was first noticed by her parents when she was about 2 years old. No such deformity was present in any one of her brothers, sisters or parents. She was married when she was 11 years of age and had her first child 9 years after the marriage. The first issue was a male child who is still alive. He is now 8 years old and possesses all the features of an oxycephalic though to a lesser degree. The frontal protuberance is slight, with moderate

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TREATMENT OF ORIENTAL SORE WITH QUINACRINE

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ORIENTAL sore is comparatively frequent in the Punjab and quite a large number of patients attending the surgical out-patients of the Mayo Hospital, Lahore, come for the treatment of this disease. These cases have been treated so far with different forms of treatment, such as the application of carbon-dioxide snow, local infiltration with berberine sulphate and hypodermic injections of the protozoal vaccine named 'Leishmin', with varying results which have been reported earlier by Warma (1931).

In 1938 Flarer in Sicily reported good results in fourteen cases with local infiltration of atebtrin.

As atebtrin was not available, treatment of these local sores was undertaken with quinacrine (M.&B. product) in the surgical out-patients, last year. The first case to receive this treatment was a young boy of 12 years who had a reddish papule at the root of the nose. The examination of the scrapings from this papule showed *Leishmania tropica*. Local intradermal infiltration with 0.1 gm. quinacrine dissolved in 1.5 c.cm. of sterile distilled water was made into and around the sore. The slight œdema which followed persisted for about twenty-four hours but without a trace of inflammatory reaction and without any noticeable pain. The sore retrogressed rapidly and when scrapings were again examined after a week, no *L. tropica* could be identified. The cure was brought about in a fortnight with a single injection. The patient on request visited the hospital on several occasions after the sore had completely healed, but it did not show any recurrence.

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exophthalmos, but the vision is normal. His mental condition is normal. The mother noticed these changes when the child was 2½ years old. About a year later another male child was born. He also showed all the features of an oxycephalic from the second year but he died at the age of 6 years of some gastro-intestinal infection. Two more children, both males, were born in succession, but they both died at a very early age before any deformity could be manifested. The fifth child who was born 18 months ago is also a male child. He has a frontal protuberance which has been noticed from his birth. Since the age of 6 months this projection has become very prominent and now he presents the picture of fully developed oxycephaly with marked exophthalmos. There is complete bilateral primary optic atrophy. The mental condition of the child is quite normal and he is fairly intelligent.

Acknowledgment

We are grateful to Colonel H. E. Murray, I.M.S., Superintendent, Medical College Hospital, for his permission to publish the case records and to Dr. K. B. Ghose, professor of radiology, for the x-ray pictures.

Encouraged by this result, treatment was undertaken in many more patients, with satisfactory results. To start with, this treatment was undertaken only in patients with one or two sores which were not very extensive, but later all types of cases were given this treatment; unfortunately this treatment had to be given up as the drug was no longer available.

In this investigation Warma's classification has been adopted, which is as follows:—

Type I—Where there is only a papule covered with reddish brown scales.

Type II—Where there is a raised area of inflamed tissue covered with scales, the latter cracked at places and exuding serous discharge, the whole surrounded by an area of chronic inflammation, but without actual ulceration.

Type III—Raised ulcerating surface, but not septic, with a hard indurated red periphery.

Type IV—Septic ulcer discharging pus, having an extensive raised base and a hard indurated circumference.

So far fifty-seven cases have been treated by this method. Before starting the treatment, *L. tropica* was identified from the scrapings in all cases except two.

In one case in which the scrapings were not examined, instead of any improvement occurring, the condition became worse and ultimately the case was diagnosed as one of seborrhœic dermatitis. Of the remaining 56 cases, only 48 could be followed. These 48 cases had 107 sores on their bodies, and the table given below shows the type of sore and the number of sores of each type which were cured by injections ranging from one to five in number.

Type of sore	Number of injections needed to effect a cure				
	1	2	3	4	5
I	14	20	26
II	2	9	8	4	..
III	16	6	4

Sores of types I, II and III were given the injections straightway, while sores of type IV were first treated with hot boric compresses and antiseptic dressings to reduce sepsis and thus converted into type III and then treated with the injections.

Technique of injections

The solution is prepared by dissolving quinaerine from ampoules in sterilized distilled water. One c.cm. of the distilled water is enough for 0.1 gm. of the drug, but for a big sore or for a case with multiple sores 0.3 or 0.4 gm. of the drug dissolved in 3 or 4 c.cm. of distilled water has been injected with impunity at one time. The syringe used is a dental syringe with a glass barrel which can inject under considerable

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NOTES ON THE CONTROL OF KALA-AZAR ON TEA ESTATES

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Introduction.—Experience and observations made in two large tea districts in Assam (East Boroï and Mangaldai) from 1926 to 1942 have convinced the writer that the several recommendations detailed below are the most

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pressure and the amount of the solution injected can be seen. Before injection, the area is cleaned with alcohol. The sore is then injected intradermally from the periphery, the whole sore being infiltrated with the solution. Generally a number of punctures are needed to infiltrate the whole sore. The injections are somewhat painful but the patients usually tolerate the pain well.

After-treatment

No special after-treatment is required in these cases. If sores are on the exposed parts like the face, after the injection the part is covered with a collodion dressing, but if the sores are on other parts, simple aseptic dressing can be given. The injections should be repeated after an interval of a week.

Conclusions

Although the number of cases treated is not very large, the series is large enough to enable us to draw important and definite conclusions:—

1. This method of treatment is very useful for sores occurring on face, lips, and other exposed parts, as it leaves no scars if ulceration has not already occurred, and very thin and small scars where ulceration has already occurred.

2. There is no inflammatory reaction after the injection, and pain after the injection is very little.

3. A number of sores can be treated at the same time.

4. This treatment can be carried out in ulcers occurring on eyelids and parts near the eye where other forms of treatment are not possible.

My thanks are due to Lieut.-Colonel V. R. Mirajkar, I.M.S., professor of surgery, K. E. Medical College, Lahore, and Dr. M. A. H. Siddiqui, Medical Superintendent, Mayo Hospital, Lahore, for their kind permission to carry out this investigation, and to my colleague Dr. A. A. Wync, P.C.M.S., for the help and suggestions in carrying out this investigation.

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necessary, practical, and productive of the best all-round results in the control of kala-azar in the many existing endemic tea districts of the Brahmaputra river valley, especially of the lower part, called by Sir Leonard Rogers and other medical pioneers 'the home' of this disease. The two above-mentioned districts are in this area, on the north bank of the Brahmaputra and at the foot of the Duffla and Bhutan hills, respectively, which are parts of the eastern extensions of the Himalayas and have all the well-known characteristics typical of ideal endemic kala-azar localities. The Mangaldai district, to which, with few exceptions, *main* reference is made in these notes, is approximately 150 square miles in area, including in this space 14 estates whose combined (planted) area is slightly over 9,708 acres.

Compressed into the limits of these estates is a coolie population, averaging (1935 to 1941) nearly 25,000 souls, and a few hundred members of the Indian clerical staffs and their families. The European population of planters and their families numbered (pre-war) 53 souls.

In its high humidity, rainfall, seasons, and other features it resembles any other tea district in the plains of Assam and therefore needs no additional description. The work of Napier particularly, and the recorded experiences of certain tea-estate medical men, *e.g.*, Dodds-Price, Percy Forster, and McCombie Young (1924) of Assam, with regard to the bad epidemics in Nowgong (Golaghat) and Sibsagar in 1914, 1916, 1918, 1920, etc., proved a powerful and permanent stimulus at the virtual beginning of the writer's career in Assam (1926), and, having been posted ever since in known endemic areas, he has had ample opportunities for observation and experiment in the control of this sometimes devastating disease. The records of such observations are set down accordingly for the benefit of those faced with some or all of the problems of kala-azar suppression in similar endemic tea districts in Assam, but who, for varying reasons, may, in some cases, have achieved only indifferent success. No attempt to dogmatize on any aspect of a necessarily complex subject is intended. The notes are offered, not without diffidence, as a narrative of personal endeavour and experience, tendered only in good faith, and for what they may be worth.

With the exception of the personal introduction of a control system and the careful compiling of graphs and statistics in the Mangaldai district, no originality of conception or of technique is claimed for the various routine and general measures discussed below.

Diagnostic and other methods for controlling the disease.—(1) In the event of an outbreak of kala-azar in epidemic form, or when a sudden and unusual rise in the incidence of the disease occurs, it is necessary first of all to take steps to diagnose all possible cases quickly. This should be done by:—

(a) Blood tests. Of these the easily-carried-out and time-honoured aldehyde test is quite satisfactory and is reliable in at least 75 per cent of cases (Napier puts it at 81 per cent) when a rough and quick mass survey is required. Further diagnostic clinical tests, such as those next to be mentioned, in suspicious cases with a negative aldehyde, can be more leisurely carried out in hospital later, if the coolie patients do not object. Among these other tests are:—

(b) Spleen, sternum, tibia, and (rarely) liver puncture. The technique of these is too well known to need description here. The warning might not be out of place, however, that no inexperienced or unskilled operator should be allowed to carry out these puncture tests, especially puncture of the spleen or liver. (Napier has over 8,000 spleen punctures to his credit however, without one mishap, which proves that in skilled hands there is little danger.) Certainly no compounder should be allowed to do spleen puncture. As the aldehyde test is generally satisfactory and simple to do, it can be carried out extensively throughout the affected estate and the whole labour force can be examined in this way in a fairly short time. Every man, woman, and child should be tested if at all possible. In this respect the writer has been, perhaps, singularly fortunate, as no undue trouble from opposition by coolies to the procedure of mass blood tests has been experienced, although, as hinted at in para. (a) above, objection is made to spleen or liver puncture. A fair knowledge of the local coolie vernacular has been helpful in many difficult situations, and is a good and requisite asset in tea-estate practice.

Should an epidemic of kala-azar assume alarming proportions, it is desirable where possible to co-opt extra medical assistance from neighbouring estates to facilitate rapid examination and preventive action.

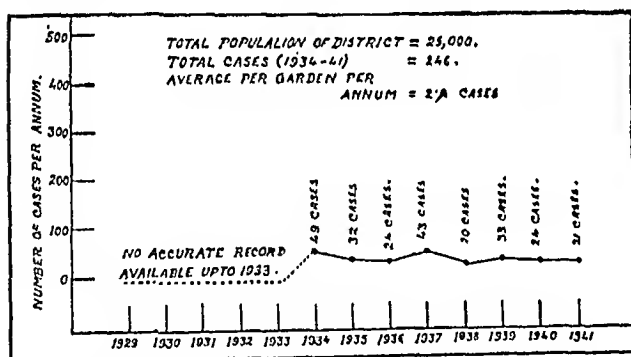
With regard to preventive measures in 'ordinary' circumstances, in gardens where the presence of kala-azar is, say, only suspected, it is a good plan to carry out, as a routine, a complete blood survey of the labour force as described above. This can be done unhurriedly by examining batches of 30 or 40 coolies a day, or more if possible, and the work can be thus completed in a few months' time without interfering with the ordinary daily garden routine work, a very important and necessary consideration which should be exercised by tea-estate medical officers at all times. All tests thus leisurely performed during the week can be set aside and produced by the estate assistant medical officer for his medical officer's inspection on the weekly routine visiting day. This assists in keeping a better check on results, and many probable fallacious reports are thus obviated. It is, in the writer's submission, a necessary and important procedure. A goodly supply of test-tubes should also be always at hand for such work. One point in addition, perhaps worth mentioning here, is that the examination of European

residents should not be omitted if kala-azar is raging in a tea estate in an endemic area.

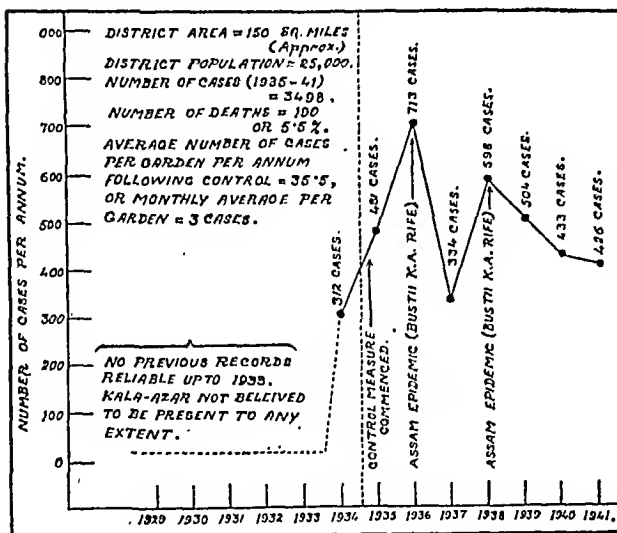
Further preventive measures are : (2) Isolation of all cases in special kala-azar wards in the estate hospital until cured; if necessary a whole family must be isolated.

(3) Mosquito nets or wire 'cages' round the beds give protection. To exclude *Phlebotomus argentipes*, nets of specially fine mesh are necessary.

(4) Thorough treatment with some effective pentavalent antimony compound is necessary. Of all drugs, until very recently, neostibosan has been absolutely unrivalled in the treatment of kala-azar in the writer's experience, with which the majority of those who have used it will undoubtedly agree. The present world war has rung down the curtain on neostibosan therapy, which is a great calamity. Other drugs are of necessity more used instead nowadays but do not bear comparison. Stilbamidine (M.&B. 744), the new British synthetic non-antimonial product, has been glowingly described recently by Napier, Sen Gupta and Sen (1942) and will no doubt revolutionize kala-azar treatment in the near future. At present, however, it is apparently only suitable for use in large hospitals with elaborate control facilities as many precautions seem necessary for its satisfactory administration.



Graph of tuberculosis in Mangaldai tea district.



Graph of kala-azar in Mangaldai tea district.

In the writer's opinion a more desirable product for Assam tea-estate practice would be a British 'fool-proof' equivalent of neostibosan. In this practice (Mangaldai), since 1935, when the writer introduced neostibosan treatment *en masse*, 3,489 cases of kala-azar have been dealt with, and a little over 80 per cent were treated by this drug, the remainder with urea-stibamine or solustibosan since the war began. Records of a large number of cases treated with neostibosan prior to 1935 in the East Boroi district are unfortunately lost, for reasons which will be mentioned later.

Of the present series of 3,489 cases the number of deaths has been only 190 or 5.5 per cent, including cases complicated with intercurrent infections, and cases which failed altogether to respond to any treatment.

(5) All contacts, *especially relatives*, should be kept under observation for 3 months. The importance of examining relatives is stressed by Napier (1927) in his textbook on kala-azar where he quotes Rogers (1910). Doubtful cases should receive at least 3 injections and be re-examined after one month and again 3 months later. The 'empirical' injections appear in many cases to have had a tonic effect and, in some, have proved diagnostic, and the treatment has therefore been pushed to a full course.

(6) All new coolies should be examined on arrival as a matter of routine, and a keen lookout maintained for old coolies under a new *alias* (a common trick) as these are sometimes suffering from chronic kala-azar.

The introduction of the disease thus from outside into a previously free garden can thereby be prevented to a certain extent, as well as a recrudescence in a garden perhaps only just emancipated from the scourge. Further, employment of *busti* (village) labour should be limited or stopped when kala-azar is known to be raging in the neighbouring villages. Cachari *busti* labour is most susceptible to kala-azar, in general experience, and can be a positive menace to recruited garden labour as 'carriers' (human reservoirs) of kala-azar (Napier, 1927).

All leave for garden coolies to visit affected *bustis* or neighbouring estates similarly affected should be also stopped and the labourers warned. The effects of nearby *busti* epidemics on the Mangaldai district estates is strikingly demonstrated in the accompanying graph. It is not suggested that the prevention of fraternizing between estate coolies and villagers is easy. On the contrary, it is the bugbear of preventive work and beyond the powers even of the Government at times, but some attempt to do so is better than none, and should be made as often as possible.

Estate managers sometimes have a wonderfully persuasive way of achieving the seemingly impossible! At any rate, 'beware the new coolie and the (Cachari) *busti-wallah*' is a safe slogan generally.

(7) Mysterious outbreaks of so-called dysentery or diarrhoea should, in the absence of other proof, be investigated by mass survey early. Many such outbreaks are in fact due to undiagnosed and untreated kala-azar. A perfectly innocent and excellent water supply in the writer's former practice (*East Boro District, Darrang*) was once condemned as the cause of a large epidemic of 'dysentery'. The manager was unshakably convinced of this and was keen to have a new water supply which was estimated to cost over Rs. 60,000.

The correct and timely diagnosis of epidemic kala-azar prevented this large and most unnecessary expense. Instead, approximately Rs. 5,000 only was spent on kala-azar treatment—to the ultimate satisfaction of the ('die-hard') manager, the directors, and certainly, the shareholders! Other occasions calling for full investigation are:—

(a) When it is reported of new coolies, particularly (*i.e.*, those of one or 2 years' residence), that, although they are known to be hard and willing workers and of good physique, they find themselves unable to finish their tasks, especially hoeing. The process is insidious and is not therefore noticed very early. The coolies affected are aware of their defection but cannot explain. (Old coolies, of course, are also susceptible.) Hookworm, vitamin deficiency from faulty diet, etc., must first be eliminated.

(b) When managers complain that many new coolies (*vide supra*), of a fine physique on arrival, begin, as it is often graphically put, to 'fade away' from supposed tuberculosis, a favourite label given by tea-estate assistant medical officers who have not had previous experience of kala-azar. One such example (*East Boro District, 1927*) of the latter category (b) was the virtual decimation, after only about 3 years' residence in Assam, of a contingent of about 300 immigrant coolies by kala-azar on an endemic estate, prior to the writer's appointment there. This was the first serious problem of his career and was just after his arrival. A spleen puncture solved the problem and saved the remainder of those unfortunate people, who were shortly afterwards repatriated as they were so utterly unsuited to the rigors of the Assam climate. It may be of interest to mention that these coolies were a mixed contingent of Kurbars, Kols, and Beders hailing from Kanara (North Hyderabad) and from Mysore. The rainfall in their country is small, only about 5 inches annually, and the climate not humid like that of Assam with its large rainfall. They succumbed to malaria, pneumonia and dysentery as well as (but most of all) to kala-azar as indicated. The choice of suitable types of labour for Assam work is an important matter to be considered when recruiting in new areas, as the loss financially to the estate proprietors can be very high if the wrong type is selected. With regard to tuberculosis, it is not so common in tea-estate practice as may be supposed. A convincing

(and typical) graph of this disease in the Mangaldai district is appended. It speaks for itself.

(8) To avoid a lot of tedium consequent on 'rush' surveys during epidemics, a good plan is to examine, as a routine, every indoor case admitted to hospital whether he is suffering from kala-azar or not. This routine examination for kala-azar leads to the compiling of records of a large number of coolies in a year, and, these records or *dossiers* being readily available, the necessity for re-examination of known cases is obviated and time saved. In any case, such a routine often reveals early cases of kala-azar and these are, so to speak, nipped in the bud, whereas, if missed, they are potential sources of danger. If a hospital case is thus diagnosed, the patient's family should be specially dealt with as mentioned in section (5) above.

Many hospital patients convalescent from pneumonia give a positive aldehyde reaction although negative previously. This was first noticed by the writer when certain cases whose aldehyde tests were forgotten on admission were subsequently done and a positive result obtained. This has led to routine re-testing of pneumonia cases during convalescence even if a negative aldehyde was found on admission. This phenomenon, doubtless observed by many, suggests that latent kala-azar predisposes to pneumonia to a fair extent by its undermining effect on the general health; but it is not proposed to discuss pathological sidelights in these notes.

(9) All cases of skin disease should be carefully scrutinized, as dermal leishmaniasis cases are very potent reservoirs of infection, more so than ordinary kala-azar cases. It has not, however, been seen frequently in the writer's practice though diligently watched for. The technique of obtaining smears from the lesions to demonstrate the parasites need not be described here.

So much for the diagnosis, treatment, and prevention of the disease itself. Now follow suggestions for dealing with the vector, *P. argentipes*.

Measures against the vector.—(1) The only way to stamp out a serious epidemic of the fulminating type is to adopt the now-topically-familiar scorched earth policy, literally (Price and Rogers, 1914). Whole coolie lines must be burned down sometimes. The coolies from the infected lines should be segregated. New lines to house them should, of course, be ready before the burning is carried out. These new lines can be safely erected as near as 50 yards from the old burned sites. This somewhat drastic procedure is nowadays, fortunately, seldom necessary, in tea-estate practice at any rate. It has only once been done by the writer in 1927 who, by quoting some of the authorities mentioned in the introduction to these notes *in extenso* to his Calcutta principals (the exact papers quoted not being remembered off hand at

present); convinced them of its urgent necessity in a certain emergency and obtained sanction for carrying out what was considered at the time to be an expensive and locally unprecedented experiment. It proved however an immediate success. But ironically enough, the writer's bungalow was accidentally burned down later (1933) and many earlier statistics and notes on kala-azar and other work from 1926 onwards were lost in the ensuing confusion, a loss not so keenly felt or realized at the time as it is at present.

(2) Jungle around coolie lines should be burnt off or otherwise eradicated by methods which will be suggested later in these notes. It is important however to *except jungle which is naturally useful for antimalarial 'shading'*, and indiscriminate clearing operations must be accordingly avoided.

(3) Where funds are not greatly lacking, wholesale prophylactic spraying is, in the writer's opinion and experience, the most effective measure possible against the vector. Spraying should be perennially carried out, and most thoroughly and systematically done by specially trained spraying squads.

Attention is invited to the following special details :—

(a) Spraying should be *regular*, once a week in the rains and once a fortnight in the cold weather. It should be done on dry days and at convenient times, *i.e.*, when the houses are opened and their occupants are at home. A locked house, with the coolie out at work, cannot be sprayed internally.

(b) All houses without exception should be sprayed.

(c) The angle between the earthen plinth or foundation of the house (inside and out), and the edges of the eaves of thatch roofs especially, must be given extra careful attention. Roof tops need not be sprayed but the whole interior of the house should be done.

(d) Other likely breeding places, *e.g.*, around the floor, plinth, etc., such as holes and cracks must be looked for and dealt with by filling when possible, or by vigorous spraying. Also the earth should be beaten hard all round the house for a few yards' radius, and any adjacent jungle might be profitably sprayed as well.

This regular spraying routine kills more than the proverbial 'two birds with one stone' in the writer's experience, and it is supported by Viswanathan (1941) in his report wherein a full account of the effects and value of house spraying is given and which shows that spraying might also be deadly to mosquitoes, eye-flies and house-flies as well as *P. argentipes*, giving a *four-in-one* effect, in fact. A number of spray solutions are on the market. Of several tried by the writer, Pyrocid 20 mixture is best and D.C.M. a good rival. Of the latter it is sometimes said that it has a strong unpleasant odour which prevents immediate re-occupation of the house after spraying. The local coolies

(*Mangaldai*) have never complained of this. On the contrary, they are said to like the odour. If houses have too many holes and fine crevices, a mixture of petrol and kerosene (half-and-half) is useful. The disadvantages are the danger of fire, and the war-time scarcity of petrol, when it certainly would not be available nor allowed to be used for such purposes. The 'Jim Dandy' sprayer solves the problem admirably, giving off a fine mist-like spray under good pressure which will penetrate the fine crevices mentioned. This sprayer and Pyrocid 20 were first suggested to the writer in 1938 by Dr. Milford Rice, former research officer, Assam Medical Research Society, Shillong, whose work is well known. His able successor, D. K. Viswanathan, agrees but also describes a sprayer he considers to be better, *viz.* Central Technical Works Sprayer (Lahore) which has been made under the guidance of the Director, Malaria Institute of India (Viswanathan, 1941a). The following solution was recommended to the writer by Dr. Strickland of the Calcutta School of Tropical Medicine and it has proved cheap and very effective. Pyrocid 20—5 parts, kerosene oil—92½ parts, and citronella oil—2½ parts. The latter mitigates the odour of kerosene. The pre-war cost was about Rs. 2-8 per gallon. One ounce was said to be sufficient for over 2,000 cubic feet. But one can be more liberal than this in its use, without being extravagant, owing to its low cost which works out to less than one rupee per day where 60 gallons average per year of solution is used. Viswanathan (1941a) gives a clear and comprehensive account of expenditure incurred on a special experiment undertaken in an Assam estate (*Limbuguri Tea Estate*) where wholesale spraying (but for antimalarial work) was done over a period of 8 months. His spray solution apparently contained no citronella oil. I give here, *verbatim*, his table of costs :—

	Rs.
'Pyrocid 20 including freight : 5.56 gallons at Rs. 43	239
Kerosene (Victoria Brand) including freight : 105.64 gallons at Re. 0-11-3 per gallon ..	75
Wages of 2 coolies at Re. 0-6-0 per day ..	161
Cost of 4 sprayers, including freight charges, etc. ..	30
Miscellaneous, bucket, drum, etc. ..	5
	Rs. 510

As the total floor area sprayed is 3,742,784 sq. ft. and cubic content sprayed is 25,010,930 c. ft., cost of spraying about 1,400 sq. ft. or about 10,000 c. ft. comes to Re. 0-3-3 1/10. The population in the sprayed group is about 950. The cost *per capita* works out as Re. 0-8-7 for spraying for the entire malarial season of a little over 8 months. (NOTE.—484 houses were sprayed.—(E. B.)

With the effective sprays available to-day, and in the absence of serious epidemics, it is not a necessary routine to condemn to burning odd coolie houses because of one case of kala-azar. In former years, doubtless an aftermath of the Nowgong epidemics scare, one wrote laconically

in the medical officer's weekly report book at the estate hospital, 'usual action please' for the manager's attention (and often to his disgust!) whenever a case cropped up, and the house was burned forthwith. This could become quite an expensive 'pastime' in a year if a lot of coolie houses were thus disposed of piece-meal. In rare instances the condemned house was sprayed instead with the unpleasant 'lime sulphur' solution, but with poor results.

A plea and a recommendation.—With regard to jungle clearing the following ideas have from time to time occurred to the writer and are now presented for digestion by any who are interested. Firstly, it strikes one that aimless and haphazard clearing of jungle often defeats its own object and results sometimes in the untidy accumulation of heaps of cut or part-burned jungle scattered all over the estate which, apart from offending the eye, is of no use at all, being merely 'matter in the wrong place'. It would no doubt be more thoroughly carried out (and the work considered less boring), especially from the view-point of the European garden staff (who are directly responsible for carrying out such schemes advised by the medical officer), if the final objective were interesting. Therefore the fairly simple, and, to the writer, practical suggestions here mentioned might be with advantage adopted as part of the future general policy of Calcutta tea agency houses. In nearly all local estates since the outbreak of war, cultivation of soya beans and potatoes has been carried out. It has been done also in many other parts of Assam, and in the process, many tracts of jungle land (e.g., lantana, thatch, argyrum, etc.) have been cleared effectively and rapidly, and also apparently without undue difficulty or expense. The agricultural transformation of the terrain concerned has been remarkable, while the remote effects, of denying, incidentally, favourable breeding grounds to numerous insect pests, are bound to be ultimately beneficial. If jungle clearing operations were extended gradually each year, the whole estate would be free in a comparatively short time. As an anti-kala-azar measure this would be effective too. Again it is apparently not very difficult to transform, in a few months, large areas of thatch jungle into tung oil gardens. This is a commonplace to-day in most districts. Further, in view of the urgent behest of various authorities, since the war broke out, to 'grow more food' (especially necessary and appropriate in such a Cinderella province as Assam), other areas of jungle in tea estates might be similarly dealt with by clearing, and then planted with fruit trees or converted into vegetable gardens, and any land that is not considered arable could be utilized as recreation grounds. In any case it is most earnestly urged that coolie lines should be kept clear and that all old, crumbling houses should be demolished too by degrees and replaced by better types. It is hoped that such plans as are suggested above will not strike any but the

greatest sceptics as being merely the Utopian wishful thinking of a 'visionary' and of no practical value at all. It is the writer's firm conviction that, if these suggestions were really given a fair trial, and an extensive one, good will accrue in full measure in a few short years and a multitude of noxious pests, most of all *Phlebotomus argentipes*, the arch enemy of many, would be compelled to seek *lebensraum* in more primeval surroundings.

Summary

1. Notes on kala-azar control methods which have proved successful in tea-estate medical practice are presented.

2. 3,489 cases of kala-azar treated mostly with neostibosan, since 1935, are quoted and this drug has been the best in the writer's experience. A plea is made for an identical British product.

3. The aldehyde test is quite satisfactory for general use and it is stressed that the medical officer should personally check all results of mass surveys.

4. The highly infectious nature of kala-azar is emphasized, and the graphs shown demonstrate strikingly the effects of *busti* epidemics on adjacent tea estates. Also, it is pointed out that Europeans are not immune.

5. Wholesale spraying is described and recommended as a powerful deterrent. It is *not* a costly procedure. The 'Jim Dandy' sprayer is favoured.

6. A plea for vigorous jungle clearing and its replacement with fruit and vegetable cultivation is seriously urged.

7. Tuberculosis is not considered to be common in tea estates in Assam.

8. Certain castes of coolies, such as Kurbars, Kols, Beders from the Deccan (Kanara and Mysore, etc.), are wholly unsuitable for work on Assam tea estates.

9. It is shown that kala-azar in the Mangaldai tea district has been kept within very satisfactory limits with the comparatively low average of 35.5 cases per annum with a crowded and potential human 'reservoir' of infection, the population numbering 25,000.

Conclusion

The large number of lives and money saved by such schemes as described is undeniably apparent. The amount of money saved and the reduction of the number of working days lost through illness per annum are most important economic factors always to be borne in mind by the tea-estates medical officer (often at the sacrifice of his own purely scientific interest) and must always be considered *first* where the commercial interests of estates proprietors and shareholders are concerned. That prevention is better than cure is also amply illustrated by these notes. Results are entirely dependent on one's own enthusiasm and perseverance and the extent

(Concluded on next page)

THE ROLE OF HORMONES IN SEX DISORDERS IN THE MALE

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Introduction

THE sex disorders of the male are, broadly speaking, impotence and sterility. Impotence means inability to perform coitus satisfactorily. The act of coitus consists, in sequence, of libido, erection of the penis, coitus proper, ejaculation and orgasm. Absence or defect in any of these factors, or disturbance in the relative time or

(Continued from previous page)

to which this can be communicated to one's subordinate medical staff, the European garden staff, and last, but certainly not least, to the several Calcutta managing agents one serves, without whose interest and co-operational support literally nothing can be achieved. No effort should be considered too great to make in this connexion, for the results often more than reward those who do not despair, even when 'facing fearful odds'.

Acknowledgments

The writer's great indebtedness to all his Indian staff for their whole-hearted help and co-operation at all times during a long association is gratefully acknowledged. Special mention of his chief assistant, Dr. K. C. Chakravarty, L.T.M. (Cal.), of Pancery Tea Estate, must be made and to whom special thanks are due for his painstaking and laborious task, for many years, of keeping voluminous and accurate data and records and for the production of the graphs and table illustrating these notes.

Finally, my thanks are due to Dr. S. R. Pandit, M.B., B.S., D.B., Director, Pasteur Institute, Shillong, for giving details of some of the references quoted.

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sequence of any one of them, constitutes impotence. Few men complain of disorder or orgasm, though occasionally some say that they do not enjoy coitus. This, when analysed, will be seen to be due to defective libido, to absence of sex attraction of the partner or to lack of adaptation between the male and female copulatory organs (e.g., as in lax vagina).

Impotence is thus not one condition but a group of conditions. Even many doctors still consider it as one condition and write prescriptions without enquiring what form the complaint takes. As a matter of fact, there is no type of physical or psychical disorder which is treated more unsatisfactorily than sex disorders.

Urologists, endocrinologists, and psychiatrists tend to attribute sex disorders to organic, endocrine or psychic disturbances respectively and treat the conditions according to their speciality.

It is generally realized that the sexual system and its functions are controlled by the mind more than any other system in the body. Nevertheless other factors cannot be ignored and the psychiatrist who minimizes the importance of organic lesions and endocrine deficiency, and tends to regard every type of impotence as primarily caused by psychic factors, will benefit from a study of endocrinology. Others who treat cases of impotence should bear in mind that the majority of cases are caused by psychic factors and a good portion of the rest are controlled by them. The difficulty is that while endocrine and organic types of impotence can be diagnosed by physical examination or laboratory tests, psychic factors cannot be gauged by any known method, and are usually detected only by a process of exclusion. Patient and tactful questioning of the patient regarding history, social condition, moral convictions, etc., will help in diagnosis. The age of the patient is important, because psychic impotence is more common before the age of thirty or thirty-five and the endocrine type in later years.

It will be shown in this paper that endocrine treatment will benefit, if not cure, a good proportion of cases of impotence even when caused by psychic factors. Failures are seen when the causes are deep-rooted psychic factors, such as inhibitions and fixations, when the only line of treatment is psychotherapy.

The endocrine factors.—The endocrine glands governing the sexual system in the male are the testes, the anterior pituitary, the adrenals, the thyroid and the thymus. The last two are of relatively little importance. The testicles are the most important. They have an exocrine function, the production of semen, and an endocrine function, the production of the male hormone. It may be noted that production of semen is dependent on the presence of the male hormone. Sperms are produced by the seminiferous tubules of the testes while the hormone is secreted, it is believed, by the Leydig cells situated in the interstitial tissue.

The male hormone.—It is now generally admitted that the male hormone brings on sexual maturity, the development of the accessory sex organs, and the formation of the male characteristics. It establishes ejaculation, controls erection of the penis, and stimulates the sex centre in the brain. In short, it develops the sex organs and initiates and controls their functions. Zelson and Steinitz (1939) are of the opinion that 'though the male sex hormone will produce an enlargement of the penis and scrotum and growth of pubic hair, it has a marked tendency to cause a shrinkage in the size of the testicle, both descended and undescended'. I have not seen this occur in my practice with the usual dosage used. It may be mentioned that after the stage of adolescence, increase in the size of the penis cannot be brought on by any quantity of the hormone administered, except in cases of sexual infantilism.

From this it is clear that in sexual infantilism and hypogonadism, the male hormone is the product to be administered. These conditions are shown by undeveloped sex organs, defective libido and erections and absent or diminished ejaculation. When the symptoms are caused by psychic factors, the male hormone acts by stimulating the sex centre, increasing the vascularity of the sex and accessory sex organs, and the quantity of the secretions of the latter.

There is no mention in the literature of premature ejaculation being caused by endocrine factors. I have suggested a possible theory later in this paper. The recognized causes of premature ejaculation are hyperæsthesia of the sex organs or prostatic urethra, prolonged abstinence and, more commonly, deep-rooted psychic causes. The use of the male hormone in premature ejaculation is justified only in cases of hyperæsthesia of the posterior urethra and adjacent areas. That it has a 'desensitizing' effect on the genital musculature is proved by its beneficial effect on the disorders of micturition associated with enlarged prostate.

Besides the action described so far, the male hormone inhibits the gonadotropic hormone secretion of the anterior pituitary. It has thus two distinct actions, a direct stimulating action on the testicular tissues and an indirect depressing action on them through the anterior pituitary—two antagonistic actions. Many observers believe that the stimulating action is only on the seminiferous tubules, *i.e.*, on spermatogenesis, and not on the interstitial tissues, *i.e.*, on the production of the hormone.

Another important factor around which controversy is still raging is the dosage level. Selye and Friedman's (1941) views may be taken as a guide for all practical purposes:—

'It also appears that these hormones (male and female) exert a direct gonadotropic action in males which is not mediated by the pituitary. All the known facts are best explained in accordance with the assumption that, in addition to this direct stimulating action, the steroids also have the property of inhibiting the gonadotropic hormone secretion of the pituitary. At

low-dosage levels, this latter action prevails in as much as small doses of various steroids, particularly the androgens, decrease gonadotropic secretion much more than can be compensated for by their direct testes stimulating effect. On the other hand, very large doses have a sufficiently pronounced direct stimulating action to compensate for the loss of pituitary gonadotropic hormone production. From this it would appear that 'if the hormonal mechanisms regulating testes function are the same in man as they are in rat and mouse, there would be less danger of damaging the testes of hypogonadal patients with large doses of androgens than with carefully administered small doses. In fact, it appears very probable that the large doses would stimulate gonadal development, or at least inhibit gonadal involution.

'It also seems likely that only the seminiferous epithelium is stimulated by large doses of androgens while the Leydig cells undergo atrophy irrespective of the dosage used. If we accept the prevailing view according to which these cells are the main source of androgen formation, this observation would be in conformity with the law of compensatory atrophy according to which overdosage with a certain hormone causes involution of the cells normally responsible for its elaboration. The fact that other steroid hormones, namely, esterone, desoxycorticosterone and progesterone, likewise result in Leydig cell atrophy, on the other hand, is an excellent example of the so-called transferred compensatory atrophy. This is an involution of endocrine cells due to overdosages with a hormone other than that normally produced by them, though usually closely related to it'.

If we analyse this statement it means that small doses of androgens deprive the testicle of the stimulating action of the anterior pituitary gonadotropic hormone but are not enough to compensate for this loss. Large doses, on the other hand, in spite of the greater depression on the pituitary, compensate and bring on the required stimulation. In other words, in castrated animals on whom the experiments were carried out, small doses were worthless while large doses alone were effective. Among human beings, the analogous cases are those of sexual infantilism and hypogonadism, and this rule should operate, and it does.

In considering high and low doses, we have to remember that these are relative terms and depend on the proportion of the dose to the body-weight of the patient. To be effective, the doses in human beings have to be very high or fairly high and administered for a prolonged period. Unless this is done, especially in sexual infantilism, no improvement will be seen. This fact should be borne in mind in treatment.

That the male hormone will not stimulate the Leydig cells to produce more of the hormone seems to be the accepted theory at present, but in my opinion it does not cause their atrophy, and when the treatment is stopped, these cells begin to function normally again unless they were completely atrophied when the treatment began. Such cases are the so-called hypogonadal cases and here my experience is that small doses will give better results and that the length of treatment needed will depend on the degree of the hypogonadism.

Large doses of the male hormone administered for a long period have a depressing effect on the sex function in sexually normal men, and in

cases of impotence not caused by endocrine deficiency. How the hormone acts in psychic cases has already been described. In these cases high doses for a short period and later small doses are advisable; otherwise the state of depression sets in and the condition is aggravated. In sexual neurasthenia, a very common condition, small doses of the hormone usually effect a cure because of its soothing effect on the brain and nervous system. Guirdham (1940) recommends testosterone propionate in the treatment of non-sexual psychoneurotic and early schizoid cases. The male hormone in addition exerts a tonic effect on the general health and body growth and weight, possibly due to its influence on the other endocrine glands. It may therefore be cautiously used in cases of general under-development (Ruhinstein and Solomon, 1941).

The anterior pituitary hormones.—The anterior pituitary gland secretes one or more gonadotropic hormones, and these are believed to initiate and regulate to some extent the functioning of the gonads. This gland influences, and is influenced by, the gonads. While some work has been done on the action of the pituitary hormone on spermatogenesis and cryptorchidism, very little controlled clinical work has been published regarding its therapeutic value in impotence.

Hormones similar to those of the anterior pituitary have recently been prepared from the urine of pregnant women and the blood of pregnant mares. Controversy is still raging as to which of these is physiologically more potent. Some clinicians are of the opinion that, because of its stimulating effect on the testicular interstitial tissues, in male sex disorders an initial course of the pituitary or 'pituitary like' hormone therapy will enhance the result of the male hormone therapy. We have to remember that all hormones are expensive and very few sufferers from sex disorders are able to spend large sums of money on these preparations. It also complicates and unnecessarily prolongs the treatment. The little experience I have of anterior pituitary hormone treatment in sex disorders makes me feel that usually its effect is purely psychic and that the same results can be brought on by any form of treatment, provided the physician has the patient's confidence; this is illustrated in the following case: A man aged twenty-six complained of feeble erections and his case was diagnosed as one of psychic impotence. He was given six injections of sterilized sesame oil every other day. It was explained to him that the product was a highly specialized and expensive hormonal one. Complete cure was effected after six injections. It may, however, be mentioned that many castrates are able to perform coitus and this is believed to be due to the action of the pituitary hormone which takes on the function of the male hormone. Whether adrenal cortex hormone can do likewise is a question which has not yet been studied.

The adrenal cortex hormone.—The adrenal cortex hormone is believed to have a physiological action similar to that of the male sex hormone in adrenalectomized animals. It is believed also that this hormone helps the foetus to develop in the direction of masculinity before the anterior pituitary is formed. The accepted theory at present is that, in the foetus, the endocrines are formed in the following order: the adrenals, the anterior pituitary and the gonads. This is the case in both sexes. The study of the adrenal cortex hormone has been confined to two pathological conditions, Addison's disease and virilism in the female. Sexual weakness and sterility are usually, though not necessarily, associated with these conditions. All cases of females suffering from virilism that have come under my notice have been sterile, though libido and menstrual function in most of them were not seriously impaired.

I have not come across any reference in the literature to cases of male virilism. By this I do not mean growth of hair on the chest and abdomen which is fairly common even in normally sexual individuals (there is a belief that such men are very virile). What I mean is cases of men having dark and long hairs, often curly, all over the trunk and limbs including the back and shoulders. Five such cases came under my notice and they were sexually weak. In one case, coitus was possible. In the other four cases, married men, the erections were so feeble that they had not consummated the marriage. They had erections, but these were feeble and the penis would not assume the forward position seen normally. This meant atrophy of the erector penis muscles, and degeneration of these muscles is one of the first effects noticed in castrates. In other words, excess of the adrenal cortex hormone has a depressing or even a destructive effect on the gonads. As I see only sexually weak cases, I cannot be sure whether all men suffering from virilism are sexually weak. The probability is that they are. Further controlled clinical studies on the subject are indicated.

The adrenal cortex hormone when present in excessive quantities has probably opposite effects in the male and in the female; in the male it acts as a female hormone and in the female as a male hormone. Selye and Friedman (1941) noticed that desoxycorticosterone, the synthesized adrenal cortex hormone, in large doses produced smaller testes and marked tubular and interstitial atrophy, if treatment was kept up for a prolonged period. I have not seen any stimulating or depressing effect in cases of sex disorders treated with this hormone. It acts as a tonic on the nervous and bodily system and thus corrects any sex weakness associated with asthenia and mental exhaustion. I have seen some rejuvenating effect when it is administered with the male hormone in elderly persons run down in health after prolonged severe mental or physical strain. Six to twelve injections every

second or third day are sufficient for the purpose. In one case I found that it decreased the craving for alcohol in a confirmed dipsomaniac.

The female hormones.—The other hormones found to be therapeutically useful in male sex disorders are the follicular and luteal hormones. 'To-day, it no longer suffices to regard the male as masculine and the female as feminine, since the two sexes have hormones of the opposite sex in their circulation and excretions... It is possible that most often they occur as inactive intermediate metabolic products but that under certain conditions they may disturb the balance of sex sufficiently to produce symptoms' (Frank, 1940).

Korenchevsky and Dennison (1937) found that the follicular hormone 'caused increase in the weight of the seminal vesicles, slight increase in the weight of the prostate; usually the penis showed no change, although there was slight increase in some cases'. Ball (1937) 'reactivated castrated male rats by the injection of estrogenic hormone... These results suggest that, in the adult male, sexual activity may be due in part, and possibly wholly, to reactivation of the pituitary which is accomplished by the estrogenic substance'.

Work on female hormones indicates that the follicular hormone exerts a direct action on the musculature of the uterus by inducing marked hyperæmia and powerful contractions. The luteal hormone has just the opposite effect. As the muscles of the female and male genital system are similar histologically and in function, similar effects are to be expected with these hormones on the male genital muscles. I have given treatment with these hormones alone or combined with the male hormone in a number of cases. My conclusions are:—

(1) The follicular hormone rapidly induces hyperæmia of the sex organs and muscles, and increases peristalsis. The secretions of the accessory sex organs are increased and the whole sexual system is sensitized. The result is stronger and more constant erections, increase in the volume of the seminal fluid, constant nocturnal emissions, quick ejaculation during coitus and increased frequency of urination. The semen is often blood stained. In other words, increased activity and sensitiveness of the sex organs are seen and these results are of the irritative type. Increased libido is also noticed and this can be accounted for by the reflex action of the hypersensitive sexual system on the brain sex centre. It will be seen that this action differs from that of the male hormone. The clinical application of the follicular hormone is thus obvious: in absent or defective erections, ejaculation and libido, especially of the paralytic type when caused by psychical factors and sexual excesses. The effect is immediate, and striking. When administered in combination with the male hormone, the secretions of the accessory sex organs are further increased, but the symptoms of irritation are not present as the

action of the latter is soothing. In sexual infantilism, the combined treatment gives better and more rapid results. The effect of this treatment in cryptorchidism and sexual infantilism is described later.

The follicular hormone is contra-indicated in all cases of sexual hyperæsthesia. It is not advisable to give large doses or prolonged treatment with small doses of follicular hormone to elderly persons because of its possible bad effects on the prostate. In one case of feeble erection in a man aged 47, I gave twelve injections of testosterone propionate 10 mg. and follicular hormone 1 mg. This effected a rapid cure without causing any prostatic enlargement.

(2) The luteal hormone has just the opposite effect and its administration is indicated in all cases of sexual hyperæsthesia, such as, increased libido, premature ejaculation, nocturnal emissions, frequent erections, spermatorrhœa and prostaticorrhœa. Also, it has a soothing influence on the nervous system. It is especially helpful in sexual neurasthenia of the hyperæsthetic type while the male hormone is indicated in cases of the depressed type.

The dosage of hormones.—Foss (1939) writes on his clinical experiments with male and female hormones in restoring the potency of a human male castrate:—

'When testosterone was used in conjunction with small doses of oestradiol benzoate, some increased efficiency was obtained, for a slightly lower threshold value of male hormone was active and emission was noted for the first time. As androgen therapy in one form or other was continued, the volume of these emissions increased; with only medium doses, such as 40 mg. per week, full erections were not possible, but when 100 mg. of testosterone propionate was given in a week in conjunction with small doses of oestradiol benzoate, erection was fully turgid. Progesterone enhanced the action of the male hormone also and one injection lasted nearly six days, whilst even progesterone alone in sufficient doses maintained potency, but the effect was not so prolonged. More recently, I have given larger doses of progesterone, 25 mg. daily, but with little effect'.

The absence of beneficial effects on potency with high doses of the luteal hormone is caused by its desensitizing effect on the sexual system. The point raised by Foss, that when two or more hormones are combined, a lower dosage of the male hormone is sufficient to produce good results, is interesting, and I have confirmed it in my practice. Also, the interval between the injections can be increased as the effect of the combined treatment is more prolonged. This reduces the cost of the treatment considerably.

I have seen no feminizing action even after high doses of female hormone given over prolonged periods. Nor has it, in my experience, increased the size of the prostate even in elderly men. Decreased libido and decreased erections are, however, noticed just as when high doses of the male hormone are administered, and this is due to the inhibiting action on the gonadotropic hormone secretion of the anterior pituitary.

A point worth remembering is that as age advances potency decreases because the production of the hormone by the testicles decreases.

'In the human individual, the microscopic studies of Moore (1936) on the prostate gland suggest a temporary flush of hormone secretion just at birth, a lower grade of secretion sufficient to cause slow prostatic growth up to approximately 10 years of age, a rather sudden onset of more active secretion at the pubertal age of 10 to 13 years, a constantly active secretion up to approximately the fifth to sixth decade and a gradual production thereafter. Some individual variation from the normal may be as great as 10 to 20 years on the decline, since prostate glands on the average show evidence of diminishing testis secretion in the fifth or sixth decade, whereas occasional individuals may present good evidence of hormone secretion even in the eighth decade' (Allen, 1932).

Thus with advancing age, decreased virility and other signs of hypogonadism are to be expected, and if these are sufficiently serious to make sex life impossible, substitution therapy with the male hormone may be resorted to. I use hormones usually by injection but applications, percutaneous and rectal, of ointments of testosterone and œstrin are efficacious when it is substitution therapy that is aimed at. A case of pronounced sexual infantilism in a boy aged twelve was cured with percutaneous application of the male hormone. When immediate results are desired, as in the psychic or paralytic types of impotence, larger doses of the follicular hormone alone or combined with the male hormone, depending on the nature of the case, should be administered. When prolonged treatment is indicated, small doses should be used. This is the procedure I follow now. Oral therapy may be resorted to in substitution therapy but very large doses will be required.

The physiological and therapeutic actions of the various hormones are described in this paper and the readers should select combinations of these to suit the requirements of their cases. The illustrative cases, few but typical, should help in deciding on the right line of treatment.

A possible endocrine theory of premature ejaculation.—Here I may be permitted to ventilate a possible endocrine theory for certain types of premature ejaculation. Excessive libido is usually associated with premature ejaculation, and excessive libido, as we have seen, can be induced artificially by the male as well as the female hormone. Premature ejaculation is often the result of an irritation and is in my opinion likely to be caused by a preponderance of the female hormone. This assumption is strengthened by the fact that, in cases of enlarged prostate, premature ejaculation is usual and one of the causes of senile hypertrophic changes in the prostate is the preponderance of the female hormone and deficiency of the male hormone, necessarily associated with advancing age. Luteal hormone, physiologically antagonistic to follicular hormone, relieves premature ejaculation and so also do small doses of the male hormone, when the disorder is not

caused by deep-rooted causes of psychic inhibitions and fixations. This theory, *viz*, excess of female hormone as the cause of premature ejaculation, may explain cases in the middle-aged and elderly persons but cannot possibly explain the cases occurring in the young. I believe that premature ejaculation in the young, when not due to organic hyperæsthesia of the sex and accessory sex organs or other recognizable causes, is always psychic. It is worth while to investigate this possible cause of premature ejaculation by estimating the relative excretion of the various hormones in the urine by quantitative laboratory tests.

Conclusion

I hope that, directly or by implication, I have not given the reader the impression that every case of sexual disorder can be cured by hormonal treatment. All that I intend to convey is that a large proportion of cases, unless they have their root in deep psychic factors, can be cured or at least ameliorated by treatment with judicious combinations of the various hormones. More important still, this paper is meant to make doctors give up the present practice of using hormones indiscriminately. No two cases are alike and it may happen that in two cases, symptomatically similar, one may be benefited by hormonal treatment while the other may not. In the latter, other lines of treatment such as psychic-analysis or urological treatment may help, but these do not come within the scope of this paper.

Illustrative cases

Case 1.—An engineer, aged 34, consulted me for nervousness and constant nocturnal emissions, the emissions occurring almost daily. He gave a history of two attacks of syphilis. Physical and serological examinations showed nothing. On enquiry it was discovered that he did not think or worry about sex and that recently had not even had erections. It was a clear case of sexual neurasthenia. The prostate was tender; the nervousness was more marked when he was in the company of others and his hand shook when he handled any instrument or even a cup of tea. Seminal emissions indicated luteal hormone treatment, but as there were depressional symptoms, including absence of erections, it was decided to combine this with the male hormone. Five mg. of perandren and 5 mg. of lutoeyelin were given on alternate days. After two injections there were morning erections, and the nervousness was better. The injections were then given every fourth day, and the dose of lutoeyelin was reduced to 2 mg. as morning erections disappeared after the third injection with the higher dose and the nocturnal emissions decreased in frequency. He felt progressively better and the nocturnal emissions occurred on the average once in 10 days. In all 12 injections were given.

Case 2.—Medical man, aged 30, and wife, aged 24, married 5 years and father of 3 children. Feeble erection and poor retentive power. Libido as usual. Had similar trouble 4 years back. Physically healthy. Diagnosis: psychic impotence.

Remarks.—The retention power might have been brought to a satisfactory level if a few injections of luteal hormone and testosterone propionate had been given after the erectile power was restored.

Days of treatment	Treatment	REMARKS
1st to 8th ..	4 injections of luteal hormone 5 mg. each	Reports slight improvement.
10th to 14th ..	3 injections of luteal hormone 10 mg. each	Condition worse, even libido less, tried coitus on my suggestion without success.
15th, 17th and 20th ..	3 injections of follicular hormone 1 mg., 5 mg., and 5 mg., respectively.	Erection definitely better and coitus possible but retentive power poor.
22nd and 23rd ..	Testosterone propionate 25 mg. each day	Erection so feeble that intromission was not possible.
27th, 29th, 31st, 34th, 36th, 38th, 42nd and 44th.	Testosterone propionate 10 mg. + follicular hormone 1 mg.	Practically normal again as regards erection. Retention power not satisfactory still.

Case 3.—Hindu, aged 26, married 3 months. Physically healthy but of neurotic temperament. During the first 3 days after marriage he had no coitus because of lack of erection. On the fourth night he had an erection but ejaculated on attempting penetration. Libido normal. Before marriage he had normal coitus twice with other women. Sex and accessory sex organs normal. Diagnosis: psychic impotence.

Case 6.—Hindu, aged 25, unmarried, complaint: nocturnal emissions, three or four times a week. Treatment as in previous case. After the treatment was discontinued, he had no emission for seven days. A curious factor was noticed while he was having the treatment, he had emissions every night.

Cases 7 and 8.—Two cases of cryptochidism were selected for treatment, one with a gonadotropic hor-

Days of treatment	Treatment	REMARKS
1st to 9th ..	4 injections of testosterone propionate 25 mg.	Reports no improvement and still unable to consummate marriage.
10th to 12th ..	1 injection daily, each of testosterone propionate 25 mg. and follicular hormone 5 mg.	Very strong erections on the 12th night and successful coitus.
14th to 16th ..	Same treatment daily	Relapse with no erection though libido continued strong.

A few days later, the patient gave up treatment.

Remarks.—This case illustrates that psychic factors are often too deep rooted to be eradicated by hormone treatment.

Case 4.—Mohammedan, aged 29, married 6 years, no children. No coitus for the last 6 months because of feeble erection. Semen dribbles out on sexual excitement. Sex and accessory organs normal. Diagnosis: paralytic impotence due to excesses.

mone (gonan) and the other with the combined male and follicular hormones. The first was a man aged 26. He was given 500 rat units of the gonadotropic hormone, thrice weekly, for 6 weeks with no appreciable result. An interesting observation was on the commencement of treatment, his sperm count was 220,000,000 per c.cm. and 10 days after the cessation of treatment it was 153,300,000 per c.cm. That those who suffer from cryptochidism have a low sperm count is thus not substantiated.

Days of treatment	Treatment	REMARKS
1st, 3rd, 5th and 7th ..	Follicular hormone 1 mg. by injection, each day.	On the 7th night he had a fairly satisfactory erection and had intercourse twice. The semen was blood stained on both occasions.
9th, 11th and 13th ..	Luteal hormone 5 mg., 2 mg. and 10 mg. by injection.	The condition worse and no erection whatever.
15th, 17th, 19th, 22nd, 24th, 26th and 29th.	Follicular hormone 1 mg. and testosterone propionate 10 mg. by injection each day.	Erectile power almost normal, coitus almost every night, some nights even twice.
33rd ..	Prescribed by mouth follicular hormone 0.1 mg. tablets <i>t.d.s.</i> and, for application on the penis, follicular hormone ointment.	

Reported one month later that his sexual powers continued to be satisfactory. In this case the luteal hormone was administered to see its physiological effect and not to benefit the patient.

Case 5.—Mohammedan, aged 23, unmarried, complaint: spermatorrhoea. Parts normal. Three injections of luteal hormone 5 mg., 10 mg. and 10 mg. every third day. Result: Complete cure.

The other was a man aged 34 years and married 12 years. His complaint was sterility. Poor erections had been noticed for 2 years. The right testicle was undescended and could be palpated in the abdomen with difficulty. The left testicle was atrophied, as a result of injury sustained 18 years previously. He showed hair growth similar to that seen in mild cases of male virilism. He had coitus once a week. The

atrophied testicle was of the size of a tamarind seed. He showed definite signs of hypogonadism. He was treated with injections of testosterone propionate and oestradiol dipropionate from 16th December, 1940 to 16th May, 1941. In all he received 1,290 mg. of the former in 100 injections. To 58 of these injections was added 1 mg. each of the follicular hormones. From the 10th injection, his erectile power and libido were increased and coitus occurred every other day. He used to get severe bearing down pain over the undescended testicle which he thought was being pushed downwards. After the 14th injection the testicle could be easily palpated and, if the internal abdominal ring had been large enough, the testicle might have descended into the scrotum. From this time his erections became feeble and libido less, obviously due to the depressing effect of the hormones on the anterior pituitary. The atrophied testicle behaved in a curious manner. It occasionally became twice its previous size and then again became small. The patient would not consent to an operation and, as no further benefit would result from the treatment, the injections were discontinued.

Case 9.—The most marked case of sexual infantilism I have come across was that of a married young man, 19 years old, with penis and testicles as infantile as those of a boy of 6 years of age. The length of the penis on erection was 2½ inches and he had no pubic hair or hair on the face. The distribution of fat in the pubic region and over the breasts was feminine in type. The general development corresponded with his age, and his weight was 120 pounds. Physically and mentally he was an adult. He reported that he performed coitus with his wife, a statement which was not supported by the latter. He was put on testosterone propionate injections of 25 mg. In 5 months he had 1,500 mg. of testosterone propionate and at the end of this period the penis on erection was 4½ inches, one testicle became markedly enlarged though the other showed only slight enlargement, pubic hair appeared, and nocturnal emissions occurred occasionally. To see whether the addition of gonadotropic hormone in the treatment would accelerate the rate of his sex development, he was put also on injections of a gonadotropic hormone (serogan) along with testosterone propionate. The only noticeable change produced by the additional treatment was that his night discharges became more frequent and more profuse. The prostate and seminal vesicles were still infantile. It was decided to have his semen tested but all that he could produce by masturbation was a few drops of urine.

The patient gave up treatment for 7 months, when he reappeared. There was no retrogression of his sex organs. His semen was examined. The quantity was 0.1 c.cm. and watery in consistency. There were no spermatozoa. He was put on injections of testosterone propionate 10 mg., and 1 mg. of follicular hormone, every other day. In all, he had 41 injections. Erections became progressively stronger and more turgid. Penis on erection was now 5 inches and he had half a dozen satisfactory coitus. The interesting point is that in spite of the large doses of the hormones administered, there was no decrease in libido or erectile power; this fact showed that, in this case of sexual infantilism androgens and oestrogens even in high doses exerted no inhibiting effect on the pituitary gland. After 15 injections, his semen was examined again. The quantity was about 2.0 c.cm. and consistency 'thinner than cream'. No spermatozoa were seen.

Summary

1. Impotence is defined and classified.
2. The physiological and therapeutic actions of the male, follicular, luteal, pituitary and adrenal cortex hormones are explained.
3. Contra-indications of the various hormones and their therapeutic indications are described.

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BLOCKAGE OF THE INFERIOR HÆMORRHOIDAL NERVE FOR OPERATION ON HÆMORRHOIDS

By E. J. RAMDAS

CAPTAIN, I.M.S.

I. Anatomy

Two sphincters guard the anal canal, the external sphincter and the internal sphincter.

The external sphincter.—The external sphincter is composed of the subcutaneous part, the superficial part, and the profundus or the deep part. The subcutaneous part is composed of muscle fibres surrounding the anal orifice, and is intimately connected with the skin. It is supplied by perineal branches of the fourth sacral nerve.

The superficial part is composed of muscle fibres which rise from the coccyx, sweep round the anus and are inserted in the perineal body. Some fibres curve round the anterior margin of the anus to form a sling. It is supplied by the inferior hæmorrhoidal and the fourth sacral nerves.

The profundus part is a true sphincter muscle. It is composed of non-striped muscle fibres. It has no bony attachment. It is in intimate contact with the pubo-rectalis portion of the levator ani. It is supplied by the inferior hæmorrhoidal nerve.

The internal sphincter.—The internal sphincter is a thickening of the circular non-striped muscle fibres of the gut, and is continuous with the circular muscle-coat of the rectum. It surrounds the upper two-thirds of the anal canal. It is supplied by the second and third sacral nerves and the hypogastric plexus.

(Continued from previous column)

Acknowledgment

I acknowledge my indebtedness to Messrs. Ciba (India) Limited for placing liberal supplies of their hormonal products at my disposal to conduct this study. The products used were *Perandren* ampoules and ointment, *Ovocyclin* ampoules, tablets and ointment, *Lutocyclin* ampoules and tablets and *Percorten* ampoules.

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The inferior hæmorrhoidal nerve from which the main nerve supply of the anal sphincter is derived traverses the ischio-rectal pad of fat and, after its exit from Alcock's canal, passes along the outer surface of the fascia lunata up to its insertion between the pubo-rectalis and the profundus part of the external sphincter. Here, about the middle of the outer surface of the sphincter, it breaks up into branches to supply the sphincter.

II. Procedure

With the patient in the lithotomy position, the perineum is painted with iodine and towels are arranged. The index-finger of the left hand is lubricated with vaseline and introduced gently into the anal orifice. The finger is then hooked over the internal sphincter, with the tip pointing towards the left side of the pelvis.

Fig. 1.—Showing the relation of nerve to sphincter. (Cunningham, Anatomy.)

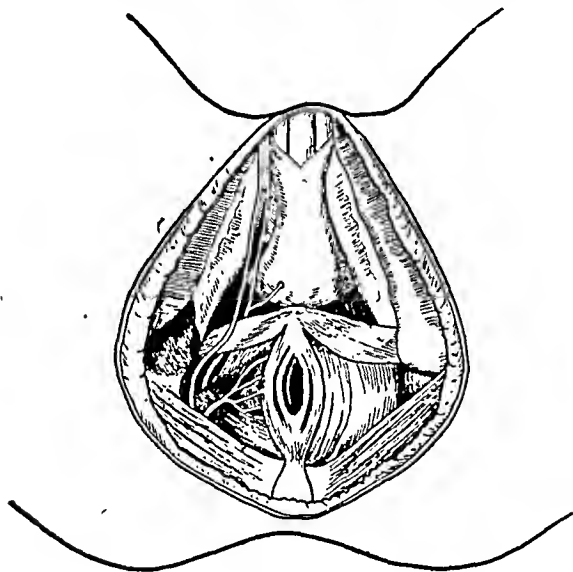
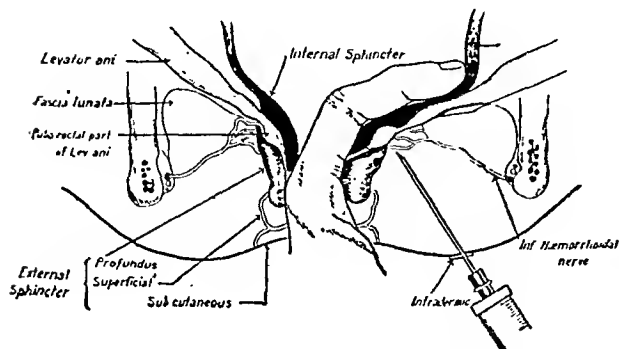


Fig. 2.



The margin of the levator ani (pubo-rectalis part) can be distinctly felt impinging against the finger. This is the place where the profundus part of the external sphincter is in intimate contact with the levator ani, and also the place where the inferior hæmorrhoidal nerve enters the sphincter. The finger inside the rectum is now so adjusted that the free margin

of the levator ani lies against the proximal interphalangeal crease.

With a fine needle on a 10 c.cm. Labat syringe (loaded with 10 c.cm. of 2 per cent novocain and adrenaline) an intradermic weal is raised, one inch to the left of anal margin, on a horizontal line passing through the centre of the anus. The syringe is so held that the tip of the needle is directed towards the middle of the interphalangeal crease.

The needle is then gently pushed in the horizontal plane, through the ischio-rectal pad of fat, which it traverses easily. A slight resistance is felt when the needle touches the fascia lunata, and the patient complains of pain. At this stage the tip of the needle can be vaguely felt by the finger in the rectum. With the needle held steady, 3 c.cm. of the solution of novocain is injected steadily, the aspiration test having been done first to avoid an intravenous injection. (There are only very small veins in the region.) A distinct bulge is felt by the finger when the injection is correctly made; at the same time the muscle is felt relaxing against the finger.

The needle is then withdrawn up to the skin and a subcutaneous weal is raised, anteriorly towards the perineal raphe and posteriorly towards the coccyx. This step is necessary only when external hæmorrhoids are present.

The procedure is repeated on the other side. Either the same finger is used or the corresponding finger of the other hand.

Within five minutes the sphincter relaxes and the operation can be started.

The mucosa of the lower part of the rectum is anæsthetized and the internal sphincter is relaxed by the solution percolating inwards.

III. Precautions

Not more than two punctures are made for carrying out the procedure, as infection is apt to occur at the point of injection.

The rectal mucosa should never be punctured.

The injection is made close to the fascia lunata. Injection into the ischio-rectal pad of fat is a common cause of failure.

IV. Advantages

The procedure is very simple, and the technique is easily learned. My colleagues who formerly operated under spinal, general, caudal, or perirectal infiltration anæsthesia have now adopted this method. Discomfort during anæsthesia is slight, and because of this, patients do not refuse operation. Adequate relaxation of the sphincters is possible without the least danger. Post-operative discomfort is very slight, as the effect of the anæsthetic lasts for more than six hours. The period of acute pain is thus tided over.

This method was worked out with the help of my colleagues, Dr. S. G. Talwalkar, now

(Concluded on next page)

INDIAN-MADE LIVER EXTRACTS IN THE TREATMENT OF MACROCYTIC ANÆMIA

By C. R. DAS GUPTA, M.B. (Cal.), D.T.M.
(From the School of Tropical Medicine, Calcutta)

I. Cipalon in macrocytic anæmia

THIS liver extract is a 'Cipla' product, prepared by The Chemical, Industrial and Pharmaceutical Laboratories, Limited, Bombay. Each c.cm. of cipalon is said to contain liver principle contained in 450 grammes of fresh liver. There is no mention of the exact Cohn fraction of liver which it contains. It is said to be sterilized by the 'tindallization' process. It was supplied to us in sealed ampoules of 2 c.cm. each.

Subjects.—Nine cases of macrocytic anæmia admitted to the Carmichael Hospital for Tropical Diseases were treated with cipalon; of these 8 were males and one a female, and their ages ranged from 18 to 40 years.

Method of administration.—Two c.cm. of cipalon were injected intramuscularly every day up to 6 days.

The injections were rather painful.

Examination of blood.—In almost all the cases a daily reticulocyte count was done from the 4th to the 10th or 12th day after the first injection and complete examination of blood was done once every week.

Results

(i) **Definite improvement.**—After injection of cipalon, definite improvement was noted in 5 cases (1, 2, 3, 4 and 5), in 3 of which (1, 2 and 3) the improvement was associated with reticulocytosis (see table A).

In 2 of these cases (3 and 4), a second course of 6 injections was given and this was again followed by definite improvement in case 3 and slight improvement in case 4. Both these patients (cases 3 and 4) were seen three months after their discharge from the hospital and were found to be completely cured of anæmia.

One patient (case 2) was improving nicely but he left hospital before the blood picture had reached the normal level, and we have no information about him since his discharge.

One patient (case 1), who was discharged improved, is reported to be sick again.

(Continued from previous page)

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I thank Professor Motwani, Grant Medical College, for his kindness in allowing me to study the exact anatomy of the inferior hæmorrhoidal nerve on the cadaver.

I am grateful to Lieut.-Colonel W. E. R. Dimond, I.M.S., Officer-Commanding, 15 Indian General Hospital and M.E.F., for his kindness in allowing me to operate on cases at the above hospital.

Case 5 showed improvement in the beginning but subsequently acid-fast bacilli were found in his sputum and he was discharged from hospital; this was thus a complicated case in which complete cure of the anæmia could not be expected.

Reactions to other liver preparations were as follows:—

Reacted to anahæmin (2 c.cm. for 6 days).	Case 4 given before cipalon
Reacted to Lilly's concentrated liver extract (2 c.cm. for 5 days).	" 4 " after "
Do. do.	" 2 " before "
Do. do.	" 3 " after "
Reacted (slightly) to T.C.F. plain liver (2 c.cm. for 6 days).	" 3 " " "

No other liver extracts were given in cases 1 and 5.

The spleen was found to be slightly enlarged in one, case 2.

Hookworm infection.—There was very slight infection in one case (3).

Indirect van den Bergh test.—In 4 out of 5 cases (2, 3, 4 and 5) the indirect van den Bergh reading was over 0.5 mg. per cent.

Sternal puncture.—In all the cases the marrow was plastic and was megaloblastic in reaction.

Gastric analysis.—Normal in 4 (cases 2, 3, 4 and 5) and hypochlorhydria in one (case 1).

(ii) **Definite failures.**—In 2 cases, 8 and 9, cipalon proved to be a complete failure. Both these cases improved later on marmite. A transfusion was given to case 8 during the course of treatment with marmite and the patient showed definite improvement after the transfusion. Case 9 had shown some improvement with iron given before marmite.

The spleen was greatly enlarged—over 7½ inches in case 9.

Indirect van den Bergh test was positive in both the cases and was over 1.0 mg. in both.

Sternal puncture.—Both showed plastic marrow, but it was only slightly megaloblastic in case 8 and normoblastic in case 9.

Gastric analysis gave results within the normal range in both cases.

Reactions to other liver preparations.—Case 8 did not respond to treatment with big doses of anahæmin (2 c.cm. given daily for 6 consecutive days), and case 9 did not respond to erythgen 2.5 c.cm. given daily for 5 consecutive days; in both the cases these liver injections were given after cipalon.

(iii) **Incomplete data.**—In the remaining 2 cases, data were not complete. Case 6 was admitted with general anasarca and a dilated heart; he failed to respond to cipalon, and later to erythgen; soon afterwards he became mentally deranged and was transferred to another hospital.

Case 7 was a relapsed case of macrocytic anæmia with a huge spleen, about 8 inches. On the last occasion, in 1939, his blood did not

improve on any liver extract but improved on iron. This time he was given a course of cipalon on which he did not show any improvement, but soon afterwards he left hospital before anything else could be tried.

Comment

Of the 9 cases, 3 ought to be left out of analysis; these were case 5 who was suffering from tuberculosis, case 6 who became mentally deranged, and case 7 who left hospital.

Of the remaining 6 cases, 4 showed definite improvement and 2 were definite failures but improved later on marmite. One of these latter did not show any improvement even on a big dose of anahæmin, which would lead one to suppose that the deficient factor which was supplied by marmite was probably absent in the liver extracts.

II. Liver extract T.C.F. in macrocytic anæmia

Liver extract T.C.F. is prepared by the Teddington Chemical Factory Ltd., Bombay. Each cubic centimetre of the injectable liver extract is said to equal 500 grammes of fresh liver. This liver extract was at first supplied in two forms, one as the plain liver extract which was supposed to be more purified than the 'G' fraction of Cohn *et al.*, which is contained in the other extract, called whole liver extract. The process of preparation, as given by Dr. B. K. Nandi, M.Sc., Ph.D., chief chemist of the Teddington Chemical Factory, is as follows:—

'To prepare T.C.F. whole liver extract for parenteral use, selected healthy young sheep livers are finely minced and added to water. The mixture is adjusted to a pH of 5.2. After sufficient stirring the mass is heated to 75°C. for half an hour and filtered. The clear filtrate is concentrated in high vacuum and at low temperature to a small volume. The inactive materials including proteins are removed by careful fractional precipitation at isoelectric point with large volumes of alcohol at low temperature. The alcoholic filtrate is tested for the absence of protein, histamine and other injurious materials and then concentrated in vacuum. This fraction contains all the active nitrogenous non-protein fraction corresponding to fraction "G" of Cohn *et al.*, besides all the vitamin-B complex of fresh liver and nicotinic acid.

The active material is dissolved in double distilled water, the reaction adjusted to pH 7.4, allowed to stand at 0°C. for a length of time, and after calculation of the final volume on the basis of the weight of liver used, 0.5 per cent of phenol is added. The solution is subsequently passed through a Seitz filter and after regular sterility tests according to T.S. Regulations filled into sterile ampoules and vials. Final sterility tests are done on 1 per cent of the filled ampoules before they are passed.'

Subjects.—Altogether 16 cases of macrocytic anæmia were treated with liver extract T.C.F.; of these, 14 were treated at the Carmichael Hospital for Tropical Diseases and the remaining 2 at the anæmia out-door clinic. Of these 12 were males and 4 females, and their ages varied from 18 to 45.

Method of administration.—Liver extract T.C.F. was injected intramuscularly in the gluteal muscles. The injections were never exceptionally painful.

Dose.—Plain liver extract was at first injected in doses of 2 c.cm. daily, but later 4 to 5 c.cm. were injected daily. The injections were given for 6 days in all cases.

The whole liver extract was always given in doses of 4 c.cm. daily for 6 days.

Examination of blood.—In all the cases complete examination of blood was done once every week and in most hospital cases a daily reticulocyte count was done from the 4th to 10th or 12th day after the first injection of liver.

Results

A. *With liver extract T.C.F. plain.*—This was tried in 8 cases admitted into hospital (see table B, cases 1 to 8).

(i) *Definite improvement.*—Definite improvement was noted in only 2 cases (1 and 3). There was no reticulocyte response in case 1, while no regular reticulocyte count was done in case 3, as the initial blood picture was high and no very great response was expected.

(ii) *Doubtful results.*—There was only slight improvement in 3 cases (2, 4 and 5); one of these, case 5, later improved appreciably on whole liver extract.

(iii) *Definite failures.*—Three cases (6, 7 and 8) did not respond at all to treatment with the plain extract; all these cases were given big doses of the extract, 4 to 5 c.cm. for 6 days; of these cases, 6 and 8 responded to treatment with other liver extracts but case 7 did not respond to any hæmatinic medication (see table below):—

Reactions to other liver extracts and hæmatinics were as follows:—

Case	Given before treatment with plain liver extract, T.C.F.	Result	Given after treatment with plain liver extract, T.C.F.	Result
1	Liver extract, T.M.	—	Campolon	+
2	Cipalon	+	Lilly's concentrated liver extract.	+
5	Liver extract, T.M.	±	Whole liver extract, T.C.F.	+
6		..	Whole liver extract, T.C.F.	+
7		..	Campolon Transfusion Erythgen	± — ±
8		..	Whole liver extract, T.C.F. Later : Cipalon Lilly Campolon Marmite Still later T.C.F. whole again.	— — — ± — +

Adren. The adren was moderately increased between 3 to 4 inches in 2 cases (3 and 4).

Haemoglobin infection. There was very slight infection in 3 cases (2 and 3), in the remaining 6 cases (1, 4, 5, 6, 7 and 8) no sign was found in the blood.

Indirect van den Berg test. The indirect van den Berg reaction was negative in 6 cases (1, 3, 4, 5, 6 and 8) and in the remaining 2 cases it was within 0.2 up per cent.

Chemical analysis. This was done in all cases except case 3. The results are shown in tabular form below:

	Alcohol soluble fraction	Water soluble fraction	Water insoluble fraction	Water soluble fraction
Number of cases	1	3	2	1
Case numbers	6	1, 2 and 5	3 and 4	7

Alcohol solubility. Alcohol solubility was done in all the 6 cases and the results were found to be positive in all. The reaction of the mixture is shown in the table below:

	Alcohol soluble	Water soluble	Water insoluble
Number of cases	4	0	1
Case numbers	1, 2, 4 and 7	3, 5 and 6	8

Reaction with liver extract. P.C.F. which gave false 11. This was found in 12 cases, of whom 10 were treated at the hospital and 2 at the out door medical clinic at the island.

Reaction improvement. Indirect van der Berg test was found in 3 out of 10 hospital cases and in both the out door cases, that is in 10 out of total 12 cases in which it was tried. The improvement was produced by administration in 4 of the hospital cases (3, 12, 13 and 14).

Three of these cases (6, 8 and 9) showing definite improvement had failed to respond to treatment with previous dose of the plain extract given earlier. Case 8 did not at first respond either to the plain extract or to the whole liver extract, but soon after showed definite improvement when the second course of liver extract with the whole liver extract was given and still later showed more improvement after a third third course.

After improvement with the first course, a short second course of treatment with the whole liver extract was given in 3 other cases (11 and 12). There was still further improvement in case (11) but no further improvement in the other (12).

Complete data. One patient (9) was included in a very long study; the results are

given a course of treatment with P.C.F. which gave correct and later liver blood transfusion and a course of treatment with cod-liver oil in spite of all treatment the patient died shortly after wards.

Other patients. One patient only (case 7) failed to respond to treatment with whole extract. The patient did not respond either to the plain extract and later he failed to respond to either cod-liver oil or syphilin.

Results in other liver extracts and human tissue were as follows:

Case num ber	When liver extract with P.C.F. was given	Result	When other liver extract with P.C.F. was not given	Result
1	1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100	1	1	1
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3	1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100	1	1	1
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21	1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100	1	1	1
22	1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100	1	1	1
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24	1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100	1	1	1
25	1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100	1	1	1
26	1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100	1	1	1
27	1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100	1	1	1
28	1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100	1	1	1
29	1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100	1	1	1
3				

Sternal puncture.—Sternal puncture was done in 7 (5, 6, 7, 8, 11, 12 and 14) of the hospital cases, in all of which the marrow was very plastic. The reaction of the marrow is shown below :—

	Megalo- blastic	Normo- blastic	Granulo- cytic
Number of cases	3	4	<i>Nil</i>
Case numbers ..	7, 11 and 14	5, 6, 8 and 12	..

Comment

Of the 16 patients, one (9) should be left out of analysis, as she was admitted in a very low condition and died within a short time after admission.

Of the remaining 15 cases, 8 were treated with the plain liver extract T.C.F. and definite improvement was noted in 2 cases only, while the whole liver extract was tried on 11 cases and in 10 of these definite improvement was noted; in 3 of these cases (6, 8 and 9) the plain liver extract had been given earlier without any beneficial result.

One patient only (case 7) did not respond either to the plain or to whole liver extract, but this patient also did not respond to campolon, erythgen or transfusion. It is to be noted (see table B) that in this patient the marrow was quite plastic and megaloblastic in reaction, and there was no absence of free HCl in the gastric secretion; on the other hand, a fractional gastric analysis showed hyperchlorhydria. This is probably one of those cases of macrocytic anæmia which do not respond to treatment with any liver preparation, though on analysis of the various factors no reason can be found for this failure. These cases may be analogous to the cases of achrestic anæmia (Israels and Wilkinson, 1936). But our investigation of this case was by no means complete, as we were unable to test the effects of marmite and other hæmatinics, since the patient refused to stay longer in the hospital.

III. Liver extract T.C.F. (plain) in pernicious anæmia

One case of pernicious anæmia was treated with liver extract T.C.F. plain, with excellent results.

A European female, aged 64, had been treated as a case of pernicious anæmia for the last several years. She was admitted into the Carmichael Hospital for Tropical Diseases in June 1941, and the investigations carried out confirmed the diagnosis of pernicious anæmia.

The patient was given T.C.F. plain, 2 c.cm. daily up to 6 days. The blood picture improved

rapidly with a reticulocyte crisis on the 7th day. A second course of three injections of 2 c.cm. each at a weekly interval brought the blood picture to the normal level (see table C).

It will thus be seen that the more purified fraction of liver, though highly efficacious in the treatment of pernicious anæmia, is not equally effective in the treatment of tropical macrocytic anæmia. This is also in agreement of our previous findings (Napier, 1941).

Conclusion

In the treatment of tropical macrocytic anæmia the results are never as uniform as in the treatment of pernicious anæmia. Accurate appraisal of the efficacy of any drug is therefore not possible. From our experience reported above we can say that the results obtained with T.C.F. 'whole liver' extract are in the same category as those we have obtained with the best crude liver extracts of foreign manufacture; it will also be seen that the results obtained with cipalon are also quite good, though not as good as those obtained with T.C.F. whole liver extract.

The results obtained however with the purified extract (T.C.F. plain) are definitely of a lower order, and not as good as those we have previously obtained with the highly purified liver fractions of the anahæmin type. But the result obtained with this purified liver extract on a case of pernicious anæmia was highly satisfactory.

Acknowledgments

This work was undertaken at the suggestion of Dr. L. Everard Napier, C.I.E., F.R.C.P., Director, School of Tropical Medicine, Calcutta. My thanks are due to him for allowing me to try the different liver preparations on suitable cases under his care at the Carmichael Hospital for Tropical Diseases and for his advice and guidance in carrying out the work and in writing this paper.

My thanks are also due to Dr. D. N. Mazumder, an employee under the Indian Research Fund Association, for technical assistance, and to Chemical, Industrial and Pharmaceutical Laboratories, Ltd., for a supply of cipalon, and to Teddington Chemical Factory, Ltd., for a supply of T.C.F. liver extracts.

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 pore, Bengal.

Number	Age and sex	Splcen	LIVER EXTRACT		HÆMOGLOBIN		RED CELLS		M.C.V.		Interval between two examinations	INCREASE OR	
			Preparation	Amount	Before	After	Before	After	Before	After		Hgb.	R.B.C.
Table A													
1	M., 38	0	Cipalon	2 c.c.×6	8.93	10.45	2.01	3.43	129.3	86.5	17 days	+ 1.52	+ 1.42
2	M., 32	2½"	"	2 c.c.×6	6.19	10.72	1.39	2.84	159.0	112.6	22 "	+ 4.53	+ 1.45
3	M., 20	0	"	2 c.c.×6	3.98	9.90	1.14	2.32	109.6	137.9	16 "	+ 5.92	+ 1.18
				2 c.c.×6	10.17	12.37	3.01	4.13	114.3	85.0	15 "	+ 2.2	+ 1.12
4	F., 26	0	"	2 c.c.×6	8.93	11.82	2.14	3.02	135.0	117.2	19 "	+ 2.89	+ 0.88
				2 c.c.×6	11.82	11.00	3.02	3.61	117.2	94.0	18 "	- 0.82	+ 0.59
5	M., 45	..	"	2 c.c.×6	3.98	6.32	1.15	2.40	161.9	108.3	25 "	+ 2.34	+ 1.35
6	M., 22	0	"	2 c.c.×6	4.53	4.67	1.14	1.35	148.0	137.0	9 "	+ 0.14	+ 0.21
7	M., 34	8"	"	2 c.c.×6	6.18	6.737	1.71	1.69	116.9	144.9	16 "	+ 0.52	- 0.02
8	M., 18	0	"	2 c.c.×6	3.08	4.13	1.31	0.98	129.8	121.2	8 "	+ 1.05	- 0.32
9	M., 26	7½"	"	2 c.c.×6	8.52	6.73	2.91	2.31	101.3	99.6	7 "	- 1.79	- 0.61
Table B													
			T.C.F.										
1	M., 45		Plain	2 c.c.×6	6.73	8.38	1.37	2.27	148.8	112.3	17 days	1.61	0.90
2	M., 20		"	2 c.c.×6	12.37	13.20	4.01	4.29	96.3	89.1	16 "	+ 0.83	+ 0.28
3	M., 30		"	2 c.c.×6	10.45	13.33	3.23	4.20	107.5	98.8	21 "	+ 2.88	+ 0.97
4	F., 36		"	2 c.c.×6	11.82	12.23	3.00	3.90	108.3	85.9	33 "	+ 0.41	+ 0.90
5	M., 36		Whole	5 c.c.×6	9.35	10.40	2.85	3.10	94.7	104.7	14 "	+ 1.05	+ 0.25
				4 c.c.×6	10.40	13.06	3.15	4.26	104.7	86.8	13 "	+ 2.66	+ 1.11
6	M., 26		Plain Whole	4 c.c.×6	9.21	9.35	2.86	2.85	99.6	91.2	16 "	+ 0.04	- 0.01
				4 c.c.×6	9.35	11.14	2.85	4.08	91.2	77.2	12 "	+ 1.79	+ 1.23
7	M., 36		Plain Whole	4 c.c.×6	8.94	8.90	1.73	1.71	167.6	157.9	10 "	- 0.04	- 0.02
				4 c.c.×6	8.90	8.25	1.71	1.77	157.9	133.4	7 "	- 0.65	+ 0.06
8	M., 25		"	4 c.c.×6	7.83	8.52	1.92	2.27	111.98	114.5	14 "	+ 0.69	+ 0.35
				4 c.c.×6	7.83	8.52	1.91	2.02	133.5	132.6	13 "	+ 0.69	- 0.11
				4 c.c.×6	10.72	14.85	2.51	4.08	127.8	93.1	25 "	+ 4.13	+ 1.57
				4 c.c.×3	14.85	16.50	4.08	4.76	93.1	90.3	15 "	+ 1.65	+ 0.68
9	F., 42		"	4 c.c.×6	3.71	2.06	0.80	0.48	138.0	166.0	7 "	- 1.65	- 0.32
10	F., 24		"	4 c.c.×6	5.08	10.03	1.18	4.06	148.3	81.2	36 "	+ 4.95	+ 2.88
11	M., 26		"	4 c.c.×6	8.38	12.70	2.02	3.96	133.6	95.9	27 "	+ 4.32	+ 1.84
				4 c.c.×3	12.37	12.50	3.61	4.85	103.8	80.4	15 "	+ 0.13	+ 1.24
12	M., 24		"	4 c.c.×6	3.98	15.40	1.02	4.54	152.0	98.2	64 "	+ 11.42	+ 3.52
13	M., 22		"	4 c.c.×6	3.98	11.27	1.02	4.92	142.1	72.1	49 "	+ 7.29	+ 3.90
14	M., 18		"	4 c.c.×6	3.16	7.01	0.64	1.75	156.2	134.3	20 "	+ 3.85	+ 1.11
15	M., 33		Ext. hepatitis liq. (T.C.F.). Whole	5i. B.D. 10	7.01	12.37	1.75	3.26	134.3	116.5	28 "	+ 5.36	+ 1.51
				2 c.c.×6	10.58	13.75	2.58	4.82	120.15	95.4	16 "	+ 3.17	+ 2.74
16	M., 56		"	4 c.c.×5	8.66	11.96	2.22	3.45	110.3	98.5	21 "	+ 3.30	+ 1.23
Table C													
	F., 64	..	T.C.F. plain	2 c.c.×6	7.56	12.51	1.59	3.64	132.1	105.8	24 days	+ 4.95	+ 2.05
				2 c.c.×3	12.51	14.71	3.64	5.07	105.8	84.2	27 "	+ 2.20	+ 1.43

BLE

DECREASE	RETICULO-CYTE		Sternal puncture	Gastric analysis	OTHER HÆMATINIC DRUGS		H.W.	V.B.	
	M.C.V.	Per cent	Day		Before	After			
- 42.8	+11.0	5th	138,000 per c.mm. Megaloblast—5.75%	Hypochlorhydria.	T.M. —	Marmite —	0	0.2	
- 46.4	+17.0	14th	Megaloblast—11%	Normal	T.M. — Lilly +	FeSO ₄ —	0	1.0	
+ 28.3	17.2	5th	115,000 per c.mm. Megaloblast—14%	Normal	—	T.C.F. plain + Lilly +	500	0.6	
- 17.8	92,000 per c.mm. Megaloblast—9%	Low normal	Anahæmin +	Lilly +	0	1.5	
- 23.2							
- 5.36	21.7	14th	167,500 per c.mm. Megaloblast—4.6%	High normal	—	—	0	1.0	
- 11.0	..		Very ill—not done	Not done	—	Erythgen —	0	Neg.	
+ 28.0	Nil		130,000 per c.mm. Megaloblast—1.4%	Hyperchlorhydria.	T.M. ±	—	400	0.6	
- 8.6	"		141,000 per c.mm. Megaloblast—6.0%	Normal	—	Marmite +	0	1.25	
- 1.7	..		134,000 per c.mm. Megaloblast—0.2%	High normal		Transfusion + Erythgen — Marmite +	0	1.25	
			Normoblast—46.4%						
36.5	Nil		Megaloblast—8%	Hypochlor.	T.M. —	Campolon +	0	1.0	
			115,000 per c.mm. Megaloblast—14%	"	Cipalon + Cipalon +	Lilly +	500	Neg.	
- 7.20	"		133,000 per c.mm. Normoblast—25%	Not done	—	—	100	0.8	
- 8.70	"		Granular—62%						
- 22.40	"		40,500 per c.mm. Megaloblast—6.7%	Low normal	Diet +	—	0	0.6	
+ 6.0			Normoblast—31%						
- 17.9	Not done		151,000 per c.mm. Normoblast—43.25%	Normal	T.M. ±	—	0	0.8	
- 8.4	Nil		170,000 per c.mm. Normoblast—35.7%	Hypochlorhydria.	—		0	1.75	
- 14.0	"								
- 9.7	Not done		220,000 per c.mm. Megaloblast—8.0%	Hyperchlorhydria.	—	Campolon ± Transfusion —	0	0.2	Left hospital.
- 19.5	"					Erythgen ±			
- 2.5	Nil		200,000 per c.mm. Megaloblast—2.25%	Absolute Achlorhydria	Before	After 1st course :	0	0.8	
- 0.9					2nd course :	Lactoflavin —			
- 34.7	6.0	10th	Normoblast—36.50%		Cipalon —	Marmite —			
- 2.8	Not done				Lilly —				
+ 28.0	Nil		Patient too weak		Campolon ±	Campolon —	0	Neg.	
- 67.2	Not done		Patient too weak	Hypochlorhydria.	—	Transfusion —	200	0.7	
- 37.7	Nil		230,000 per c.mm. Megaloblast—21%	Low normal	T.M. +	—	0	0.8	
- 23.4	"		164,500 per c.mm. Normoblast—70%	Normal	—	—	0	1.0	
- 53.8	15.0	5th	Not done	Low normal	—	Ferrosol +	1,600	1.75	
- 70.0	8.0	6th							
- 31.9	20.0	10th	110,000 per c.mm. Erythroblast—17.0%						
- 17.8	Nil		Normoblast—38.6%	Not done	—	—	2,400	0.4	
- 26.7	Not done		Not done	"	—	—	0	Neg.	
- 11.8	"		"	"	—	—	0	0.4	
- 2.63	+16.3	7th	45,000 per c.mm. Megaloblast—13.4%	Absolute Achlorhydria	—	—	0	0.5	
- 21.6	Nil								

A ROTARY RACK FOR DOING THE WEIL-FELIX REACTION

By INDERJIT SINGH

MAJOR, I.M.S.

INDER SINGH

MAJOR, I.M.S.

and

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INSTEAD of the ordinary rectangular rack, a circular rotary rack has been used by us. The experimental tubes are rotated alongside the control tubes. The light comes from below after being reflected from a black surface. The readings are very clear and can be quickly made without disturbing the tubes.

The rack consists of two circular plates of wood (figure 1) about 7 inches in diameter, and perforated near the margin by a double (or triple)

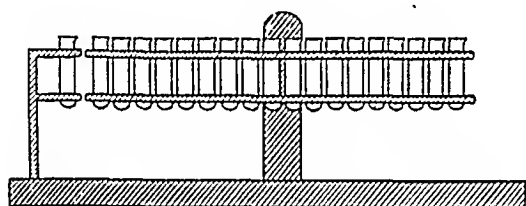


Fig. 1a.—Lateral aspect.

row of holes to fit the test-tubes, $\frac{1}{4}$ inch apart. The holes in the lower plate are smaller than those of the upper ones to prevent slipping of the test-tubes. The distance between the plates is 1 inch. Any size can be made to suit requirements. The circular plates are mounted on a stand 2 inches high, and which is fixed on a rectangular wooden

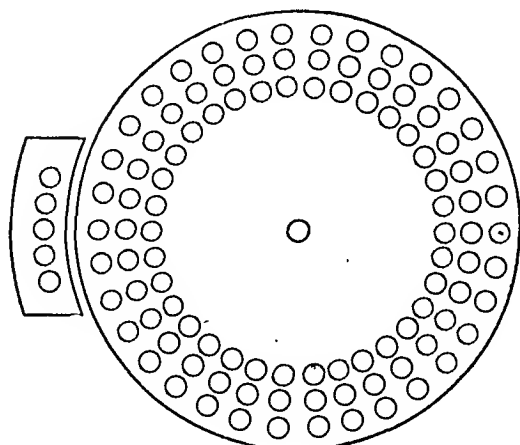


Fig. 1b.—Upper aspect.

base about 8 inches square. The base is painted black on the upper surface to facilitate readings, or readings can be made by slightly tilting the rack. The control tubes are kept on a stand fixed on the base by the side of the rotating circular plates and perforated by five holes for test-tubes for Rv, Vi, Ao, Bo and To.

(Concluded at foot of next column)

TOXICOLOGY OF YOUNG SHOOTS OF COMMON BAMBOOS (*BAMBUSA ARUNDINACEA* WILLD.)

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THE young shoots or sprouts of common bamboos (*Bambusa arundinacea* Willd.) are used as food and taken in most parts of India either as pickles or as a curry. During the rainy season they begin to come out from the roots of mature bamboos and then become available in the vegetable stalls in the bazar. They are taken by all classes of people and have lately become popular even among the European residents in Calcutta. Cattle are also fond of these shoots and the owners of bamboo clumps always try to protect the young shoots by fencing off the clumps during the rains when bamboos begin to sprout. The shoots are always found covered with coriaceous sheaths which fall off when they grow larger and maturer. They are soft and edible when they are about 20 to 25 inches in height.

Fatal cases of cattle poisoning by bamboo shoots are of frequent occurrence in Bengal as the village people know well to their cost. Cases of human poisoning are also known to the toxicologists of this country, but the actual poison which causes symptoms of poisoning or death has not yet been traced and there is much speculation about its chemical nature. The fact that the shoots are cooked by boiling in plenty of water accounts for the rareness of poisoning in man.

In a previous investigation it was established that hydrocyanic acid, present in the form of a cyanogenetic glucoside in *Sorghum vulgare* (called *juar* in Hindi and *gama* in Bengalee) at certain stages of its growth (Bagchi and Ganguli, 1941), is responsible for quite a large number of deaths of cattle in Bengal and Bihar and possibly in other provinces. As both sorghum and bamboo belong to the same natural order, *Gramineae*, it was thought worth while extending the scope of that investigation to include bamboo shoots with a view to finding out if both contained the same cyanogenetic glucoside which liberates free hydrocyanic acid under certain conditions.

(Continued from previous column)

The experimental tubes can be arranged in groups respectively of Rv, Vi, Ao, Bo and To; or the different tubes can be arranged in the same series as the control tubes. More than one test can be done on the same rack, so that it is labour-saving.

It was discovered that by simply soaking the mashed pulp of the tips of bamboo shoots in plain water for about two hours and then acidifying and distilling it, as was done in the case of *Sorghum vulgare*, varying amounts of HCN were obtained from bamboo shoots of different sizes and species. The tip or the growing point of the shoot was found to yield the maximum amount of HCN, while the base (with the roots) and the intervening portions yielded much less. The shoots, which are young and of vigorous growth and do not exceed 18 inches in height, are very rich in HCN. The following table gives an idea of the HCN content of the different parts of the shoots of various sizes and species. Each shoot was divided into four equal portions and examined separately with the results shown in the table :—

enzyme normally present in the same tissue but not in the same cells.

In vitro the hydrolysis takes place in two stages and at the first stage the products are only glucose and *p*-hydroxy-mandelo-nitrile, $C_6H_4(OH).CH(OH)CN$. The latter does not split into hydrocyanic acid and *p*-hydroxy-benzaldehyde but is hydrolysed into *p*-hydroxy-mandelic acid, $C_6H_4(OH).CH(OH).COOH$. This fact shows that there exists much difference between the normal enzymic hydrolysis which takes place in the stomach and the artificial hydrolysis by strong acids or alkalis effected in the laboratory.

The complete hydrolysis of the glucoside by its specific enzyme and the production of maximum amount of HCN are brought about when the bamboo shoot is made into a pulp and soaked in plain water for some time (about two hours).

TABLE

Number of the sample	Size and species of the shoot	Portions of the shoot from base to tip	Percentage of HCN (after pulping and soaking in water for 2 hours)
1	<i>Balcooa</i> bamboo shoot (the commonest species in Bengal)— Height .. 10 inches Maximum diameter .. 5 "	1st portion (base with some roots) 2nd portion 3rd portion 4th portion (tip)	0.098 0.250 0.570 0.80
2	<i>Balcooa</i> bamboo shoot— Height .. 12 inches Maximum diameter .. 5 "	1st portion (base) 2nd portion 3rd portion 4th portion (tip)	0.112 0.314 0.580 0.680
3	<i>Balcooa</i> bamboo shoot— Height .. 18 inches Maximum diameter .. 4.5 "	1st portion (base) 2nd portion 3rd portion 4th portion (tip)	0.109 0.266 0.362 0.422
4	<i>Balcooa</i> bamboo shoot— Height .. 8 feet Maximum diameter .. 4 inches	1st portion (base) 2nd portion 3rd portion 4th portion (tip)	0.103 0.288 0.412 0.520
5	<i>Tulda</i> bamboo shoot— Height .. 20 inches Maximum diameter .. 5 "	1st portion (base) 2nd portion 3rd portion 4th portion (tip)	0.098 0.201 0.276 0.350
6	<i>Tulda</i> bamboo shoot— Height .. 24 feet Maximum diameter .. 3 inches	1st portion—at the 8th foot from the base. 2nd portion—at the 16th foot 3rd portion—at the 20th foot 4th portion—at the 24th foot (tip)	<i>Nil</i> 0.151 0.231 0.324

As hydrocyanic acid plays an important rôle in plant nutrition, and as it is always found in combination with glucose and other organic compounds known collectively as aglucones, a careful search was made for a cyanogenetic glucoside which on hydrolysis would give rise to HCN. By using suitable solvents, the glucoside was isolated and found to be identical in chemical composition with that obtained from *Sorghum vulgare*, $C_6H_4(OH).CH(CN).O.C_6H_{11}O_6$. It is composed of glucose, HCN and *p*-hydroxy-benzaldehyde. It is very rapidly hydrolysed into its components by the specific

Identical conditions are obtained in the stomach (abomasum) of cattle where the absence of free HCl contributes to the hydrolysis of the glucoside of the masticated shoot by the specific enzyme present in the same mass.

As the presence of acids or alkalis prevents the enzymic hydrolysis of such glucosides (Bagchi and Ganguli, 1939) the human stomach is not the ideal place for the production of maximum amounts of HCN. Moreover the usual methods of cooking destroys the enzymes and prevents the hydrolysis to a considerable extent,

(Concluded on next page)

TESTS WITH MEPACRINE HYDROCHLORIDE, B.P. AGAINST *PLASMODIUM RELICTUM*

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THESE tests were made with the object of ascertaining the curative value of a substitute for atabrin, mepacrine hydrochloride, B.P. (Bengal Chemical and Pharmaceutical Works, Ltd., Calcutta), in experimental malarial infection of canaries due to a strain of *P. relictum*. Five female canaries were used in the experiments. Of these, one bird died during the incubation period of the infection and a second died just after the first appearance of parasites in the peripheral blood, and before treatment. These two birds are therefore omitted from further reference. The report deals with the three remaining birds.

Methods.—The infections were induced by intramuscular inoculation of parasitised blood from an artificially infected sparrow. The birds were treated after the appearance of parasites in the peripheral blood, but before the acute stage had developed. If treatment is left to a later stage it may be difficult to say whether a reduction in the number of parasites is due to the action of a drug or to the natural recovery which is usually evident in infections with this strain of *P. relictum*. The dosage employed was 5 mg. per 20 g. of body-weight of bird; this dose was found by Tate and Vincent (1934) to be the maximum dose of atabrin tolerated by canaries

(Continued from previous page)

and this is the reason why human poisoning is comparatively rare. The pickled shoots, which are not usually boiled, may prove fatal to a human being if taken in excess, or insufficiently cooked curry retaining the enzyme and unhydrolysed glucoside may undergo complete hydrolysis in the human stomach if the HCl content of the gastric juice is considerably reduced.

It is stated that 20 grains of anhydrous hydrocyanic acid are fatal to a full-grown bullock or cow (Linton, 1927); therefore about 5 to 10 ounces of a bamboo shoot yielding 0.8 to 0.4 per cent of HCN may cause death in about two hours. The minimum fatal dose of anhydrous HCN in man is about one grain, which may easily be obtained from a quarter of an ounce of uncooked shoot or a slightly larger amount of insufficiently cooked shoot.

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for several consecutive days. The birds used in the present experiments each weighed 16 g. so that the dose of the substitute drug was 4 mg. The drug was dissolved in 0.5 c.c. of distilled water and introduced into the crop through a catheter tube attached to a syringe or pipette.

Blood films were examined daily till the infections became chronic and thereafter at varying but frequent intervals. The parasites were counted against 500 red blood cells if numerous, or against 1,000 cells if scanty, and the density estimated per 10,000 red blood cells.

Results. Experiment 1.—Two canaries (birds nos. 460 and 461) were inoculated with equal quantities of infected blood from the same donor sparrow at the same time. Both birds were positive four days later, the parasites being very scanty (less than 10 per 10,000 red blood cells) in each case. No. 460 was treated on the first and second days of the patent period. By the third day, the blood was negative and the treatment was stopped. At no time was the infection more than very scanty, the parasites never numbering more than 10 per 10,000 red blood cells. The blood was still negative, fourteen days after treatment. No. 461, which was kept as a control and untreated, showed parasites continuously for eleven days, when it unfortunately died, though probably not as a consequence of the malarial infection, but from some other undetermined cause. The parasite numbers during the acute stage ranged between 500 and 1,080 parasites per 10,000 red blood cells. Thus the drug administered as soon as the parasites appeared in the peripheral blood appears to have prevented the development of the acute stage in no. 460 and reduced the patent period of the infection by at least nine days.

Experiment 2.—Bird no. 462 was treated from the third day of the patent period, or roughly at the commencement of the acute stage. The parasites then numbered 360 per 10,000 red blood cells. On the fourth day of the patent period, after one dose had been administered, an increase in the number of parasites was noted: the figure was 660 per 10,000 red blood cells. But it was observed that about 50 per cent of the parasites were abnormal in morphology. These abnormalities will be described presently. On the fifth day, after the second dose, the number had fallen to 280 parasites per 10,000 red blood cells, with a considerably higher proportion of degenerating forms. On the sixth day, after the third dose, the number was 60 parasites per 10,000 red blood cells, again degenerating forms predominating. The bird was found dead the next day, twelve days after inoculation. In a fifteen minutes' search of the heart blood, only one normal-looking parasite, a gametocyte, was observed. The cause of death, which was in all probability not malaria, is unknown. It would appear that the acute stage was suppressed and the infection controlled, though for want of an immediate control bird, this opinion is partly based on previous experience with this strain of parasite.

In addition to its effect on the character of the infection due to *P. relictum*, it is believed, from the abnormal morphological appearances observed, that the drug has a destructive action on the parasites of this species. Thus, the parasites may appear as small, rounded bodies, barely recognizable as malarial parasites. Trophozoites and schizonts may be badly stained, abnormally vacuolated, or deficient, and even completely lacking in pigment. Gametocytes may show aggregation of the pigment similar to that normally characteristic of mature schizonts. These abnormal appearances were noted in both the treated birds.

Comments

There are few observations on the curative value of atabrin in infections of *P. relictum* with

(Concluded on opposite page)

A MODIFIED MEDIUM FOR ISOLATION OF DYSENTERY, ENTERIC AND CHOLERA ORGANISMS

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Introduction

MACCONKEY'S bile salt lactose agar has been used for many years for the isolation of pathogenic organisms (excluding *V. cholerae*) from stools, but often it has been found not completely satisfactory, especially for the dysentery organisms, and various attempts have been made to find a better medium.

The chief recent development has been the use of media of the selective type, i.e., the media

(Continued from opposite page)

which to compare the results obtained with the substitute drug. Kikuth (Bishop, 1942), Kikuth and Giovannola (1933), and Tate and Vincent (1934) have investigated mainly the prophylactic action of atebirin. Kikuth (*loc. cit.*) found that atebirin caused a temporary disappearance of parasites from the peripheral blood, but the infection was not eradicated. Tate and Vincent (*loc. cit.*) report that when a four days' treatment was commenced at the height of an infection, the parasite level soon fell until only very few parasites were present two days later; but the blood was still infective to a clean bird. They also noted morphological changes in the asexual forms. These became vacuolated and devoid of pigment. The substitute drug is shown by the tests reported above to be similar to atebirin in its effect on the asexual forms. The abnormal distribution of the pigment noted in many gametocytes may also signify anti-gametocytic properties. Whether the substitute drug has overcome the infection or not, in bird no. 460, is not yet clear.

The tests although extremely limited in number and scope have provided encouraging results which warrant further trials in both avian and mammalian malaria. It may be stated that a few tests against *P. gallinaceum* in fowls have given similar results.

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Later note.—One additional bird infected with *P. relictum* developed a patent infection, and was treated in the same way with the same results as birds 460 and 462, but thirteen days after the disappearance of parasites, the blood was infective to a clean bird. This fact indicates that the treatment does not eradicate the infection.

which favour the growth of pathogenic organisms and inhibit the growth of coliform organisms. Two selective media used for the isolation of dysentery bacilli are the desoxycholate citrate agar medium, and *Shigella-salmonella* agar (S S agar) medium as prepared by the Difco laboratories. Another medium, the tellurite iron rosolic acid medium, is recommended by Wilson and Blair for isolating *Bact. flexneri* only.

Desoxycholate citrate agar.—Leifson (1935) used desoxycholate media composed of sodium citrate, sodium desoxycholate, ferric ammonium citrate, neutral red and agar, and found them to be superior to non-selective media for isolation of dysentery bacilli. Paulson (1937) used the above media and found them useful. Irons *et al.* (1939) compared MacConkey's bile salt agar with desoxycholate citrate agar and found the latter superior to the former for the isolation of dysentery bacilli. Coleman (1940) however showed that desoxycholate citrate agar inhibited some strains of *Bacterium shigae* and he was therefore of the opinion that the medium was not reliable for isolation of all types of dysentery bacilli.

Shigella-salmonella agar.—Recently the Difco laboratories have prepared this selective medium, and Mayfield and Gøber (1941) have reported very good results with the use of this medium. Of the 1,062 samples of stools examined by these authors, 379 samples were positive for dysentery bacilli on S S agar and 356 on desoxycholate citrate agar. Thus they found the S S agar superior to the desoxycholate agar.

Pot (1942) used 'Bacto' SS agar for the diagnosis of bacillary dysentery. He isolated mainly *Bact. flexneri* and Schmitz's bacillus and *Bact. sonnei* from a few cases but no *Bact. shigae*. The formula given by Pot is that of bacto-dehydrated S S agar plus brilliant green added to it. Rose and Kolodny (1942) used the same formula with brilliant green added and reported good results in isolation of *Bact. flexneri*. They have found S S agar superior to desoxycholate citrate agar. Difco laboratories admit that 'Shiga strains do not readily develop' on their S S agar.

Present work

Experience with S S medium.—Since desoxycholate was not available, and since the medium was found inferior to bacto S S agar by some of the above workers as it did not allow the growth of all Shiga strains, we worked with only the S S medium.

As all bacto-labelled constituents were not available, we prepared a medium with our own stock of reliable ingredients following the formula given by the Difco laboratories and found that, although dysentery bacilli could be isolated from artificial mixtures of coliform and dysentery bacilli, coliform bacilli were not

markedly inhibited and some Shiga strains were inhibited.

Moreover the colony size of dysentery bacilli was small. Hence the medium was not entirely satisfactory. Also the formula quoted by Pot (1942) and Rose and Kolodny (1942) incorporating 0.00033 per cent brilliant green in the medium was found by us entirely unsatisfactory. Brilliant green markedly inhibited the dysentery bacilli.

Modification of the S S medium.—We tried modifying the formula of S S agar and our inoculum consisted of several loopfuls from a test mixture of 10 to 20 c.cm. of young broth culture of *Bact. coli*, 1 c.cm. of culture of *Bact. aerogenes* and 1 c.cm. of broth culture of dysentery bacilli. By repeated trials and modifications we found the following formula, with the addition of a buffer in the form of sodium phosphate, effective for the isolation of not only the dysentery bacilli but also enteric organisms and vibrios. An addition of 0.2 per cent sodium sulphite favoured the growth of *Bact. coli* and hence it was discarded. It was also found that the presence of three sodium salts, namely sodium taurocholate, sodium citrate and sodium thiosulphate, and of ferric citrate was essential for inhibiting the growth of *Bact. coli* and other lactose fermenters. Iron citrate scales on the other hand favoured the growth of dysentery bacilli. The presence of the buffer was favourable to the growth of the dysentery, enteric and cholera organisms and also increased the period of usefulness of the medium to about one week. A

Constituents of the modified medium

Lemco (Oxo. Ltd.)	0.50	per cent.
Peptone (Difco)	0.50	" "
Sodium taurocholate (Smith Stanistreet and Co., Ltd.)	0.85	" "
Sodium citrate (Merck)	0.80	" "
Sodium thiosulphate (Merck)	0.85	" "
Sodium phosphate (Merck)	0.75	" "
Ferric citrate (Smith Stanistreet and Co., Ltd.)	0.30	" "
Lactose (Merck)	1.25	" "
Agar	2.50	" "
Neutral red 0.25 per cent (Grubblor and Co.)	1.5	c.cm. to 100 c.cm.

Mode of preparation of the modified medium.—A stock sterilized mixture of lemco, peptone, bile salt and plain agar at pH 7.0 is prepared and kept ready. To 100 c.cm. of this stock melted, sodium citrate, thiosulphate, ferric citrate and neutral red in requisite quantities are added. 0.5 c.cm. of 2N. NaOH is then added to make the final pH 7.4. The medium is then sterilized by boiling for two minutes, and poured into plates.

Results with the modified medium

(i) *Artificial mixtures of cultures of coliform organisms and pathogens found in stools.*—The results of experiments with artificial mixtures are given in a summarized form below. Ten parts of *Bact. coli*, one part of *Bact. aerogenes* and one part of either dysentery, enteric or cholera organisms, were mixed together before plating.

TABLE

Nature of inoculum	Growth on D.E.C. medium	Growth on MacConkey's medium	Growth on Difco dehydrated S S agar
<i>Bact. coli</i> and <i>Bact. aerogenes</i> + <i>Bact. shigae</i> .	<i>Bact. shigae</i> , about 20%	<i>Bact. shigae</i> , nil	<i>Bact. shigae</i> , about 10%.
<i>Bact. coli</i> and <i>Bact. aerogenes</i> + <i>Bact. flexneri</i> .	<i>Bact. flexneri</i> , about 20%.	<i>Bact. flexneri</i> , one or 2 colonies only occasionally.	<i>Bact. flexneri</i> , about 10%.
<i>Bact. coli</i> and <i>Bact. aerogenes</i> + <i>Bact. typhosum</i> .	<i>Bact. typhosum</i> , about 95%.	<i>Bact. typhosum</i> , about 1 to 5% only.	
<i>Bact. coli</i> and <i>Bact. aerogenes</i> + <i>Bact. paratyphosum</i> A or B or <i>Bact. typhi murium</i> or <i>Bact. enteritidis</i> .	Salmonella, almost 99%	Salmonella about 1% only.	
<i>Bact. coli</i> and <i>Bact. aerogenes</i> + <i>Vibrio cholerae</i> , Inaba subtype.	Inaba sub-type pure, 100%.	Nil, lactose fermenters only.	Inaba sub-type, about 20%. Colonies firmly adherent.
<i>Bact. coli</i> and <i>Bact. aerogenes</i> + <i>V. cholerae</i> , Ogawa subtype.	Ogawa sub-type pure, 100%.	Do.	Ogawa sub-type, about 20%. Colonies firmly adherent.
<i>Bact. coli</i> and <i>Bact. aerogenes</i> + <i>V. El Tor</i> .	El Tor pure, 100%	Do.	
<i>Bact. coli</i> and <i>Bact. aerogenes</i> + Paracholera and saprophytic vibrios.	Vibrios, pure 100%	Do.	

medium two weeks' old was found to favour the growth of lactose fermenters and hence was unsuitable. On account of its usefulness in isolation of dysentery, enteric and cholera micro-organisms, we have named this medium the D.E.C. medium.

As Difco dehydrated SS agar was not available in sufficient quantity, we could not try it with all our artificial mixtures. Plating with coli-dysentery mixture was repeated by adding 20 parts of *Bact. coli* and one part of dysentery organisms but still the growth of *Bact. coli* was

markedly inhibited and dysentery organisms were easily isolated.

Pot's formula for S S agar with brilliant green was tried, but dysentery, enteric and cholera organisms did not grow at all on this medium.

(ii) *Artificial mixtures of normal stools and cultures of intestinal pathogens.*—Very small quantities of young broth cultures of organisms were added to normal stools rendered faintly acid or alkaline to litmus paper and a few loopfuls from such mixtures were plated. Such a procedure was adopted as stools from all types of cases were not easily available. Moreover we considered it essential to see whether intestinal pathogens could be isolated from known mixtures before we would try actual pathological materials. The results are given below in a table.

Experiments were repeated with D.E.C. medium four days old and S S agar prepared according to the formula given by Difco laboratories and it was found that, although dysentery and enteric organisms could be isolated on the latter, practically no vibrios were seen growing on this medium. Moreover, the S S agar medium prepared with 1.7 per cent agar was so soft that we had to increase the agar to 2.5 per cent.

The above table shows that D.E.C. medium is superior to all the rest. Organisms of the dysentery, salmonella and vibrio groups can be isolated with ease on this medium. The medium is clear and translucent and shows no contamination when kept in the incubator for days.

It may be noted here, that colonies of *Bact. sonnei* were colourless on the new medium.

TABLE

		D.E.C. medium	S S agar prepared with the strength of agar increased from 1.7 to 2.5 per cent	MacConkey's bile agar	Lactose litmus agar	Wilson-Blair (old) medium
Acid or alkaline stool + F ..	F	+++	+++	—	+, one colony.	..
Do. + S ..	L	+	++	+++	+++	..
	S	++++	+++	—	+, one colony.	..
Do. + Sn ..	L	+	++	+++	++++	..
	Sn	++	+	++	++	..
Do. + T ..	L	+	+	++	++	..
	T	+++++	+++	+	+	+
Do. + A ..	L	+	+	+++++	..	+++
	A	+++++	++++	++	..	Bile salt agar
Do. + V.C.	L	+	+	++++
	V.C.	++++	±	+
Do. + NAG	L	+	+++	++
	NAG	+++	+
Do. + E ..	L	+	++
	E	+++	+
Acid or alkaline stool + F, T and V.C. mixed.	L	+	++
	..	F, T, V.C. all isolated from the same plate.

V.C.=*V. cholerae*; E=*V. El Tor*; F=*Bact. flexneri*; T=*Bact. typhosum*; A=*Bact. paratyphosum* A; S=*Bact. shigae*; Sn=*Bact. sonnei*; NAG=Non-agglutinating saprophytic vibrios; L=Lactose fermenters.

Isolation was almost equally easy from slightly acid or alkaline stools. As controls, stools were also plated on the above media without adding any micro-organisms, but no pathogenic organisms were found. Stools mixed with enteric organisms were also plated after enrichment in tetrathionate broth on freshly prepared Wilson-Blair medium as modified by Tabet (1938), but there were a few colonies only mixed up with other organisms at the original site of inoculation after 48 hours of cultivation and the rest of the plates was almost free from any growth. Another objection to Wilson-Blair medium is that there is always a practical difficulty in getting the plates ready at will and that plates prepared must be used on the same day.

For the isolation of vibrios, it is superior to bile salt agar which is largely used in Calcutta. Vibrio colonies were characteristically transparent with slight opacity in the centre, and much bigger than colonies of dysentery or typhoid organisms.

(iii) *Dysenteric stool.*—One hundred and thirty-two samples of stool were examined microscopically and by cultural methods. In 66 samples, cellular exudate and mucus were present.

	D.E.C.	MacConkey's agar
Mucus and cellular exudate present in 66 samples	22	3

Dysentery organisms were isolated in 22 samples out of 66 on D.E.C. medium and in 3 samples only on MacConkey's bile salt agar.

Bact. flexneri, *Bact. shigae*, and the Newcastle bacillus were the dysentery organisms that were isolated. *Bact. morgani*, *Bact. asiaticum*, *Bact. alcaligenes*, *Bact. pseudocarinatus*, *Pseudomonas pyocyanea*, etc., were also isolated from several samples.

(iv) *Enteric stool*.—Sixty-nine samples were examined. *Bact. typhosum* was isolated from 11 samples on D.E.C. medium and 2 samples only on MacConkey's agar.

(v) *Cholera stool*.—As the epidemic subsided when we started our work, only 12 samples of cholera stool were examined and the result on the D.E.C. medium was highly satisfactory. Coliform organisms were very few and there were many colonies of vibrios on each plate. On the other hand, colonies of vibrios were very few on Difco S S agar. On bile salt agar medium, colonies of coliform organisms were preponderant, and colonies of vibrios were much less numerous than on the D.E.C. medium. We hope to give a further trial on this new medium during the next cholera epidemic and compare its usefulness with that of Aronson's and modified Wilson-Blair media.

Summary and conclusions

The new medium, named D.E.C. medium, modified from Difco S S agar is found highly suitable for the isolation of dysentery, enteric and cholera micro-organisms and other lactose non-fermenters from stools and from artificial mixtures of normal stools and intestinal pathogens.

The medium is very clear and retains its usefulness for about a week after it is prepared and poured into plates. Contamination of plates with fungi, spore-formers, etc., is rare.

MacConkey's bile salt agar being definitely found inferior to D.E.C. medium is now to be abandoned in favour of the D.E.C. medium in this institution.

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A Mirror of Hospital Practice

LUNG ABSCESS ASSOCIATED WITH THROMBOSIS OF VEINS OF NECK AND ARM

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Case history.—A Hindu male, aged 35 years, was admitted into Krishnarajendra Hospital on 10th September, 1942. His complaint was that he was suffering for the past six months from cough, pain in the chest, irregular attacks of fever, foetid expectoration and progressive emaciation. For the past fortnight the right upper extremity had progressively increased in size. Of late he was feeling breathless even while at rest and was unable to lie down. He had lost all appetite, was not getting any sleep and for a few days past was having diarrhoea.

Clinical findings.—The patient is very much emaciated and anemic. He is dyspnoeic. Tongue is dry and furred, skin dry, expression anxious. Pulse is rapid and thready. The right upper extremity is oedematous throughout its entire length (figure 1).

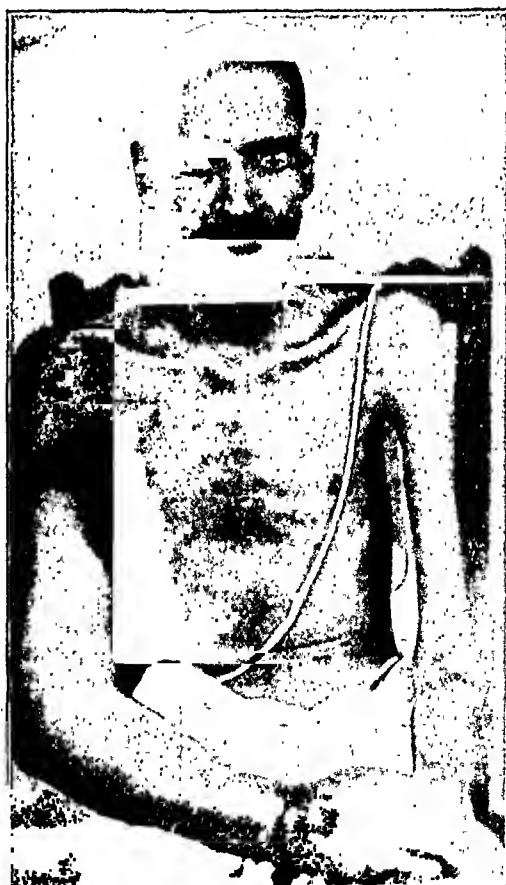


Fig. 1.

The trachea is displaced to the left of the middle line of the neck. The right external jugular vein is thick and cord-like on palpation. The veins over the chest on the right side are prominent and tortuous.

The spleen is enlarged about 3-fingers' breadth below the costal margin and slightly tender. The liver is not palpable.

The right side of the chest appears full as compared with the left. Respiratory excursion is considerably diminished over the left side. Percussion note is hyper-resonant over the right and impaired over the left side, tending to be flat towards the left base. Vocal fremitus is considerably diminished over the left side. Respiratory murmur is normal over right side and distant over the left side. A few medium sized râles are audible over left supra-spinatus region. Vocal resonance is almost lost over the lower half of the left lung.

The apex beat is not visible but is faintly felt over a wide area in the fourth intercostal space and $\frac{1}{2}$ inch outside the mid-clavicular line. The area of deep cardiac dullness extends almost to the anterior axillary line to the left; the left border of the heart cannot be made out distinctly. Heart sounds are audible over all the valvular areas, the second sound being accentuated in the pulmonary area.

The patient is intelligent and answers questions properly. Pupils are normal and react to light and accommodation. There are neither motor nor sensory changes. All reflexes are normal.

Pathological findings.—No abnormality was detected in the urine and stool. Blood for malaria was negative, microfilaria positive. Kahn and Kline tests were negative. Sputum—tubercle bacilli not found; elastic fibres present.

Radiological findings.—There is a big abscess occupying almost the entire lower lobe of the left lung with the shadow of the fluid level and prominent in its middle (figure 2).



Fig. 2.

Post-mortem findings.—The patient died 30 hours after admission into the hospital and his body was subjected to a post-mortem examination.

The abdominal contents do not present any evidence of inflammatory changes, either tuberculous or otherwise, and the omentum, intestines, appendix and mesenteric glands appear normal. The spleen is adherent to the diaphragm, is enlarged and shows evidences of perisplenitis. There is a large white infarct involving the entire upper pole. The rest of the cut surface is reddish brown and reveals prominent fibrous trabeculae. The liver is not enlarged, is pale in colour and suggestive of fatty liver. The kidneys are not enlarged, appear congested and the capsule strips easily. On section, the cortex is clearly demarcated from the medulla. The pancreas, supra-renals, bladder and ureters are normal.

Thoracic contents.—Heart: The left half of the pericardium is adherent to the chest wall by means of fibrous bands; transverse diameter of the heart *in situ* is 10 centimetres. The pericardial sac contains $3\frac{1}{2}$ ounces of sero-sanguineous fluid with a few flakes of fibrin floating in it. Epicardial fat is well preserved. The great vessels are full of dark clots. The superior vena cava, right innominate vein, right internal jugular, right subclavian and right axillary vein are thrombosed and are felt as hard thick cords. Veins around the tracheal artery are also thrombosed. The chambers of the heart contain pale clots. There is slight hypertrophy of the left ventricle. Valves are normal and coronary arteries are patent.

Lungs.—(i) Right: Adherent to the diaphragm by means of dense fibrous bands. There are two small infarcts in the lower lobe. The right pleural sac contains 17 ounces of straw coloured fluid. The right lung is oedematous. On section and pressure frothy fluid exudes.

(ii) Left: Completely adherent on all sides to the chest wall and to the pericardium. It is removed piecemeal with difficulty. It is collapsed. There is a large abscess involving the greater part of the lower lobe: it contains greenish yellow pus of an extremely fetid odour.

Cranium.—Not opened.

Discussion

It is evident from a consideration of the above facts that the patient died as a result of a severe toxæmia secondary to a chronic lung abscess and that he had developed thrombosis of the veins of neck and arm. There are two possible explanations of this condition. The one is that an abscess in the lung formed first, probably after an attack of pneumonia. The abscess became progressively bigger and resulted in severe toxæmia. A process of endophlebitis set in as a result of toxæmia in the veins of the neck and arm which in turn gave rise to thrombophlebitis of the above veins, or the severe toxæmia so greatly undermined the general condition that a 'marantic thrombus' was formed in the neck veins (Boyd, 1938). The second alternative is that the patient had some infection of the middle ear which developed into thrombosis of the lateral sinus, later spreading into the internal jugular vein. A septic embolus detached itself from this and caused septic embolism of the pulmonary artery which in turn resulted in infarction and later abscess of the lung (Boyd, 1940). It will now be interesting to determine which of the above two courses is the more probable one. In trying to come to a conclusion certain difficulties arise which have also to be properly explained. Taking the patient's history into consideration it would appear as though the patient had been suffering from the lung condition longer than the neck and arm condition. Also the nature of the abscess, i.e. single, big, and basal, points to its formation being due more to a pneumonic process or to inhalation of septic material (Boyd, 1940). Literature on the subject, so far as we know, nowhere mentions thrombosis of neck and arm veins setting in as a

complication of lung abscess. The second alternative that the lung abscess formed due to dissemination of septic emboli from a thrombosed lateral sinus has much support from literature on the subject (Ida, 1938; Cantele, 1937). But if this explanation is presumed, two anomalies will have to be explained. First, the absence of any history suggestive of middle ear disease or lateral sinus thrombosis. Second, embolic abscesses are small and multiple (Ackermann, 1939) and not single and big as the one we are dealing with.

In the absence of definite data as to the condition of the middle ear, nasal sinuses, lateral sinus and the brain, we cannot decide which of the two courses actually occurred in our case. Taking into account the consensus of opinion among leading pathologists and the presence of infarctions of the other lung and the spleen, the thrombosis of the internal jugular vein and the lung abscess might have originated from an undiscovered middle ear infection leading to a lateral sinus thrombosis.

We wish to offer our grateful thanks to Dr. Robert Heilig, first physician, Kirshnara-jendra Hospital, for his kind encouragement and valuable suggestions while writing this paper and to Dr. V. R. Naidu, pathologist, for kind permission to publish extracts of the *post-mortem* report.

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MALARIAL URTICARIA—TWO CASE REPORTS

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URTICARIA as a result of malarial infection is a rare occurrence. This is similar to urticaria due to other diseases; its diagnosis is likely to be missed by many unless laboratory help is available. Two such cases are reported below :—

Case 1.—On 6th August, 1942, morning, a male child, two years of age, was shown to me, complaining of fever preceded by chill and rigor and accompanied by urticarial rash all over the body since the previous night.

On examination the following were noted :—

Temperature 102°F. Pulse 130 and respiration 32 per minute; spleen 2 fingers below the costal margin; liver

not enlarged; urticarial rash all over the body; bowels moved; blood—malignant tertian rings found.

Treatment.—Quinine hydrochloride grains 1½ by mouth thrice daily and an alkaline mixture three times daily. The same afternoon temperature was normal; rash subsided.

On the following day temperature normal, no rash, blood negative.

The boy was given quinine and alkaline mixtures thrice daily for another five days, and since then he has remained well.

Case 2.—A coolie boy, ten years old, attended the outdoor dispensary on 10th August, 1942, morning, for the treatment of fever preceded by chill and rigor, and urticarial rash all over the body with excessive itching since previous night.

On examination I found : Temperature 101°F., pulse 120 and respiration 30 per minute, spleen 3 fingers below the costal margin, liver not enlarged, bowels clear, urticarial rash all over the body, blood—malignant tertian rings found.

Treatment.—Quinine hydrochloride grains 2½ by mouth with an alkaline mixture thrice daily. Afternoon temperature normal, rash disappearing except over the abdomen. At night the temperature rose again with chill and rigor with the reappearance of similar rash all over the body.

On the following morning temperature 99.2°F., rash in same condition as in the previous morning, blood showed malignant tertian rings.

Treatment.—Quinine hydrochloride grains 5 intramuscularly and alkaline mixture thrice daily. Afternoon temperature 98.6°F. Rash same, at night there was rise of temperature again.

On 12th morning—temperature 98.4°F., rash markedly diminished, blood—malignant tertian rings—a few.

Treatment.—Quinine hydrochloride grains 5 intramuscularly and alkaline mixture thrice daily. Afternoon temperature normal, rash—only over the abdomen. Quinine grains 3 by mouth.

On 13th morning and evening temperature was normal, rash completely disappeared, blood negative.

Treatment.—Quinine 2½ grains by mouth with an alkaline mixture thrice daily.

Summary and conclusion

Two cases of malarial urticaria, successfully treated with quinine and alkaline mixture, are reported. Both of them showed hypersensitivity to malaria parasites in an hyper-endemic area. In case 2 the rash did not disappear while the peripheral blood showed malaria parasites and the temperature continued. It is likely that with the sporulation of malaria parasites in the circulation a definite but unknown product is liberated which causes allergy resulting in urticaria.

Acknowledgment

My thanks are due to my chief Dr. N. G. Moitra and Mr. W. D. Simpson, manager, Telepara Tea Estate, for their favour of permitting me to publish the above notes.

[*Note.*—The rationale of the method of quinine administration in the second case is not clear. There appeared to be no indication for intramuscular injections.—EDITH, I. M. G.]



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Indian Medical Gazette

JANUARY

PERIPHERAL NEURITIS

DURING the evacuation of Burma, a large number of soldiers and civilians had to tramp some hundreds of miles in very rough country; many were subjected to considerable hardships including a gross insufficiency of food. Some of these evacuees arrived in India in a deplorable physical condition and obviously undernourished, and it was not unnatural that medical men attending them readily diagnosed specific nutritional deficiencies in these subjects. A condition suggestive of the polyneuritis of beri-beri was noticed on some of the evacuees, and this condition was put down to vitamin B₁ deficiency.

A number of persons with this label came into the hospital attached to the School of Tropical Medicine for further investigation. Whilst there was no doubt that the majority of these patients had been on a very defective diet, there were others with a similar condition whose diet had not been particularly deficient, at any rate not markedly deficient in vitamin B-complex. It therefore seemed necessary to consider other causes for the multiple neuritis displayed by these patients.

Many of the causes of toxic neuritis could be excluded, e.g., alcohol and lead, but amongst those that had to be considered was diphtheritic neuritis. In the absence of any history even suggestive of faucial diphtheria in any of the cases, or even amongst other evacuees, this possibility might also have been discarded, except for the fact that all—as well as some other patients, who were not evacuees but had been trekking in the Assam Hills, with the same condition—gave the same history of having suffered from sores on their bodies and limbs within the previous few months. These sores were usually described as Naga sores.

The causal organism of these so-called 'Naga sores' is a fusiform bacillus which is usually present in association with a spirochæte, and also very frequently with a diphtheroid organism. This diphtheroid does not appear to be itself capable of causing an ulcer, for its experimental inoculation does not cause a sore, at least it did not in the cultures we have investigated, but it is possible that in other Naga sores the true Klebbs-Loeffler bacillus may sometimes become engrafted. In an investigation carried out at the School of Tropical Medicine some years ago on two patients sent down from the Chittagong Hills (the same group of hills through which many of the evacuees trekked), with the story that the ulcers they displayed were typical of a special type of ulcer that was

common in these hills, and popularly known as *garigha*, it was found that there were no fusiform bacilli present, but that the main organism isolated from the sores in both patients was a diphtheroid, indistinguishable from *Corynebacterium diphtheriæ* both morphologically and culturally; this organism when injected produced local lesions from which it could again be recovered. These ulcers were not typical Naga sores, but they certainly bore little similarity to the shallow veld sore, which is now recognized as being caused by *C. diphtheriæ*.

The causal organism of veld sore is considered to be the true Klebbs-Loeffler bacillus, and it is recognized that these sores often appear in epidemic form, that they may be associated with epidemics of faucial diphtheria, that they respond to local treatment with anti-diphtheritic serum, and that they may be followed by a temporary peripheral neuritis.

Peripheral neuritis has not been described as following Naga sore, but the writer has seen a few cases in which this sequel occurred. Moreover those people who normally have these sores are primitive people who do not readily attend hospitals or come under accurate observation, and it is possible that peripheral neuritis is not so rare a sequel to Naga sore as it appears to be.

The diphtheria toxin is absorbed at the site of the lesion, passes up the afferent nerve fibres to the cord and/or brain, where it first affects the motor cells, then diffuses to neighbouring cells, and is finally distributed widely by the blood, so that there are at first paralyses of the muscle groups in the vicinity of the local lesion, and then of neighbouring groups, and finally both sensory and motor fibres of other nerves are affected. These sensory changes are often overlooked, as children, who form the bulk of patients with faucial diphtheria, are naturally not so conscious of them.

In the Burma evacuees, sensory changes were very prominent and in a few cases seemed to be unaccompanied by any motor defects, but in all the worst cases, paresis was also very prominent.

Another point was the late appearance of the symptoms and the fact that they did not always seem to appear first in the limbs where the ulcers were, but again this was usually the history obtained when the patient was questioned carefully.

The Schick test was done in several of our patients, and without exception the result was negative, a finding which is in keeping with the suggestion that they had had a diphtheritic infection recently.

In all the patients seen by us (and all the others about whom we have been given details), the condition improved steadily, whatever the treatment given. It seems very doubtful if the large quantities of vitamin B₁ given to these patients affected the rate of progress.

It would be interesting if the bacteriology of the ulcers could be studied more carefully and all

diphtheroids identified accurately. Next rainy season will probably afford an opportunity for such a study.

Further, as Naga sore is always with us, it is to be hoped that clinicians will make careful

enquiries regarding the occurrence, or otherwise, of these neurological complications amongst sufferers, especially those who live in, or near, the range of hills that separates Assam from Burma.

L. E. NAPIER.

Medical News

INDIAN MEDICAL SERVICE (E.C.) PROMOTION TO RANK OF MAJOR

THE Government of India have decided, with the approval of the Secretary of State for India, that Emergency Commissioned Officers of the I.M.S. of 10 years' standing or more shall be eligible for promotion to rank of Major. The period of 10 years shall include, in addition to previous full pay qualifying commissioned service, any period of antedate that may be granted to an individual officer.

Credit for previous commissioned service and antedate shall be subject to a maximum of 10 years.

Hitherto only doctors recruited as specialists among the Emergency Commissioned Officers in the I.M.S. have been eligible for promotion to the rank of Major.

THE MENACE OF THE HOUSEFLY

FLIES are generally known to be carriers of disease, but not many people in India realize the full extent of the menace. Houseflies can be carriers of such intestinal diseases as typhoid, cholera and dysentery and also probably help to spread other diseases including tuberculosis and ophthalmia. The nature of the threat to human health from houseflies and the manner in which these pests can be controlled are explained in a small bulletin 'The House-Frequenting Flies, their Relation to Disease and their Control' by Dr. I. M. Puri of the Malaria Institute of India, which has been published by the Manager of Publications, Delhi, as Health Bulletin No. 31.

After some introductory passages dealing with flies and their habits and showing by means of illustrations how they spread disease, Dr. Puri explains how various house-frequenting flies can be identified. He next shows how these creatures act as carriers of various diseases and goes on to explain how the threat can be averted by preventing egg-laying and breeding and by the use of screens and by trapping and killing adult flies.

It is hoped that this bulletin, which is available from all sellers of Government of India publications at six annas a copy, will be of use not only to Public Health officials but also to the general public.

MALE NURSES FOR MILITARY HOSPITALS: IMPROVED TERMS OF EMPLOYMENT

LAST April the Government of India in a press note announced their intention to recruit male nurses for military hospitals during the present emergency.

They are now pleased to announce improved terms and conditions of recruitment in respect of this category of medical personnel. The scale of pay has been raised from Rs. 50-5-75 to Rs. 75-5-100 with an additional emergency allowance of Rs. 25 per month. Male nurses will be given the rank of Warrant Officers, Class I, in the Indian Medical Department and on appointment will also be entitled to travelling allowances as for second grade officers.

CIVILIAN DOCTORS IN MILITARY HOSPITALS: REVISED RATES OF PAY

IN November 1941 the Government of India announced their decision to recruit civilian doctors (licentiates) for duty in military hospitals in India, on a salary of Rs. 100 per month (consolidated) for those employed in one military station, and Rs. 120

per month (consolidated) for those employed for duty in one military district.

They have recently considered the question of an improvement in the salary of those doctors and are now pleased to announce that with effect from 23rd October, 1942, civilian doctors (licentiates) employed in one military station will be granted a salary of Rs. 120 per month (consolidated) and those employed in one military district Rs. 160 per month (consolidated).

PREPARATION OF DRIED BLOOD PLASMA IN INDIA

EXPERIMENTS which have been carried out with improvised desiccating machines in Bombay and Calcutta show that dried blood plasma can readily be manufactured in India and that, provided sufficient donors come forward, there is nothing to delay production on a large scale as soon as the desiccating machines which have been ordered from America, and one of which has already reached India, are installed.

The Calcutta experiment with a locally improvised machine was carried on at the All-India Institute of Hygiene and Public Health with funds provided by the Indian Research Fund Association. In Bombay the Haffkine Institute has set up a similar improvised machine, the funds for this having been provided by the local Government. The amount of dried blood plasma that these two machines are turning out is small but the experiment has served a useful purpose.

The first machine received from America has been set up in the All-India Institute of Hygiene and Public Health, Calcutta, and the second, when it arrives, will be placed in another suitable centre, and it is estimated that these two machines can produce over 100 pints of the dried product every week. It will only remain for donors to come forward in sufficient numbers for large-scale production to begin.

The preparation of blood plasma in the dried state, as is well known, is a highly technical process which enables the essential elements of blood to be preserved practically indefinitely and to be transported safely to any part of the world for use.

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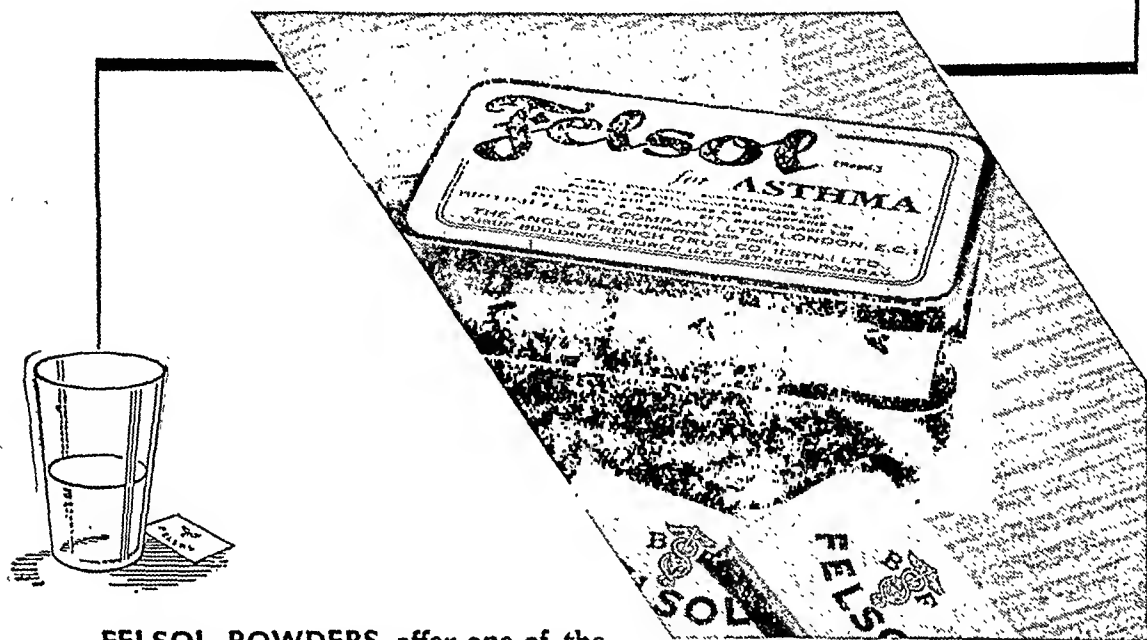
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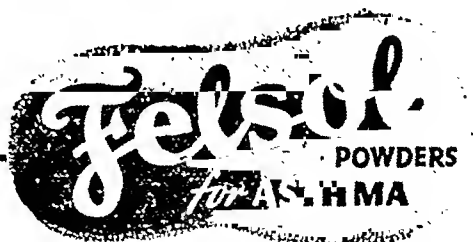
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Public Health Section

PUBLIC HEALTH ORGANIZATION

VI. THE HEALTH OF THE SCHOOL CHILD

By KHAN BAHADUR ABDUL HAMID, B.Sc., M.B., B.S.,
D.P.H., R.C.P.S. (Eng.)

*Assistant Director of Public Health, Hygiene Publicity
Bureau, U. P.*

No apology is needed for the selection of this title to this paper. Sir George Newman, formerly Chief Medical Officer of the Board of Education, England and Wales, originally gave this title to his annual reports on the subject of the medical inspection of school children and the teaching of hygiene in schools, and a more succinct, yet comprehensive, title has not been found for it. From Dr. W. P. Jacock's analysis of an ideal public health organization, which has recently been published in the *Indian Medical Gazette*, it would appear that a good medical officer of health is one who combines in himself some heterogeneous qualities, and this is all the more necessary in a country where public opinion in health matters needs a considerable amount of moulding. An officer who places health education in the forefront will be most valuable and he will find that the most interesting part of health education is school health work.

School health work is of recent origin; it was almost unknown in India about 20 years ago. Since then the scope of work in different parts of the country has been so limited and it has varied so much that it is difficult to show any very tangible result of the efforts made, although there are many individual instances of good work. The experiments that have been tried over this long period have however served the purpose of crystallizing opinion on the methods of working and administration. The problem of preventive medicine demands a wide outlook and the prevention of disease conditions is possible if steps are taken at the early stage of life. The main objects of school health work are to detect tendencies to physical defects in the school child and correct them. This is therefore one branch of modern public health work which leads towards treatment in its broad sense, a branch with which the department of public instruction is directly concerned. The health of the school child being the basis on which the health of the nation is built, school health work should be a primary concern of the State.

During the period of experimentation it must have been an interesting experience for the member of the medical department who was transferred first to the public health department which in its turn placed him at the disposal of the education department to conduct the school

work under the ægis of the public health department. In another province the medical department lent its officers directly to the education department, without the intervention of the public health department, to conduct the work more or less on their own; and in a third province the education department, having for some time attempted to do the work on its own, passed it entirely over to the public health department which created the school health officer. For administrative purposes it would be correct to place the agency for looking after the health of the school child directly under the education department, otherwise the officers have no standing in schools; but if the education department has no chief medical officer having a public health outlook, there can be no means of co-ordination and guidance on the technical side. The formation of a separate service on these lines has been recently suggested by the Central Advisory Board of Health, and this would be effective if promising officers of the public health department are deputed to the new service for periods of five years, with the head of this department to act as the chief medical officer of the education department. It will be noted that under such a system the agency doing the school health work will assume the conservative but appropriate title of School Medical Service, while the work retains an intimate association with the agency for preventive medicine.

The school medical work is the most interesting branch of preventive medicine, but medical inspections made for the purpose of collecting and tabulating records are of little use, if adequate provision is not made for the follow up and correction of defective conditions. The absence of such provision has been the main cause of the uncertain progress of the scheme. Specialization in school medical work is well within the reach of the average medical man, but he has to guard himself against falling into the rut of routine inspections. Interest in the work is created and maintained if it is felt that day by day a new generation is passing through one's efforts into better conditions; and most certainly, if it is remembered that, with a little initiative, the field for research work widens immensely, as there is scarcely any other branch of preventive medicine with greater scope for investigation and research. The employment of part time workers is not to be encouraged as the nature of the work demands the undivided attention of a type of medical man who would himself grow with the growth of the system.

The life of the school child when he is most susceptible to external influences can be divided into two stages, the stage of primary education and the stage of secondary education, and the ideal system of medical inspection should be

such as to embrace both stages. Educational institutions are of various kinds, and the one called the Anglo-Vernacular High School which provides for the population in urban areas, and which takes a child from the upper primary stage to the high school stage in eight years, is to be given first consideration, as it is in this type of institution that the continuity of education is maintained with consistency. Ordinarily a whole-time school medical officer should be able to examine in detail each year 3,000 children, the scholars being examined on admission as new entrants, in the middle of their career, and on leaving. This number will be provided by a school population of about 8,000 children, who will be found in about 20 institutions in a fairly large town.

As measures for the correction of defects should be based on education, the same officer should hold charge of a school clinic that should be located in a central place, for the correction and treatment of the defective conditions which he has found at the inspections, and it should open on Sundays and public holidays in the morning, to enable parents to attend and consult the school medical officer about their children. In the absence of a system of follow up by school nurses (health visitors), the adoption of which system in the existing condition seems to be a remote possibility in this country, the central school clinic has been found to serve fairly well this useful purpose. It is also at the clinic that defectives are sorted out for institutional treatment, and through it arrangements should be made for surgical and other treatment that may have to be given in a hospital. The clinic should be provided with facilities for the special treatment of the conditions of the teeth, eye, ear, nose and throat, and for this purpose the co-operation of honorary dentists and ophthalmologists should be enlisted, at least in the larger towns, and it may be necessary to defray their conveyance expenses.

It is at this stage that a liaison with the medical department becomes imperative for consultative work and institutional treatment of the defectives sorted out at the clinic. The school medical work is one branch of preventive medicine which cannot be regarded as a departmental activity, on account of its close interrelationships with other branches. It is not the sole concern of the education department, it is linked up with the public health department and it has to form an alliance with the medical department; it should therefore be conducted in conjunction with all the three by the formation of a co-ordination committee at the centre, as recommended by the Central Advisory Board of Health. If the State is to bear the expenses of finding out defects which retard the educational progress of children, the parents should shoulder the financial responsibility for the correction of defects. They should be charged,

for the maintenance of the school clinic, a sum of one anna per head per month, not as a separate fee for medical work but in consolidation with the tuition fee, so that their children may have the privilege of free medicine for minor ailments at the clinic, free treatment for minor dental defects, free testing of their eyesight and free inoculations to protect them from cholera or typhoid, besides health education which is the essence of all corrective treatments for the defects revealed by routine inspections at regular intervals, defects which, if left unattended to, would be prejudicial to scholarship. The medical fee *per capita* suggested above would be roughly one half of the total cost of the comprehensive scheme. Such a comprehensive scheme of medical inspections is operative in one province.

It has been observed that the educational aspect of treatment is apt to be neglected if there is an attendance of more than 30 children per day even at a well-equipped clinic. Not more than 8,000 children should be allotted to a whole-time school medical officer, as in practice he will find it necessary to incorporate in the scheme some subsidiary work which will also take part of his time. He has to co-operate with the physical instructor; train some of the teachers to give regular treatment on school premises to children suffering from trachoma and enlargement of tonsils, children whose daily attendance at the clinic may not be necessary; hold special lectures in schools on delousing if an epidemic of typhus is feared; give a series of lectures on the subject of school inspection to pupil-teachers in the training college of the town; give talks on the importance of the Junior Red Cross work; act as a judge in a competition on first aid; give magic lantern lectures on general hygiene; advise on the setting up of a health exhibition at school functions; or attend a conference of teachers.

In smaller towns where there is not enough work for one whole-time officer, the scheme outlined above may well be introduced with a little modification. Two or three small adjacent towns may be under one officer who should visit each town in turn for several days at a time; the clinic also may be of itinerant nature. Obviously this cannot be a very satisfactory arrangement, as the clinic work would be best appreciated if it is a permanent fixture, but this drawback can to some extent be overcome by enlisting the assistance of school teachers who should be encouraged to continue the clinic work during the absence of the school medical officer from the area. The visit of an ophthalmologist and a dentist should be arranged for, on payment, at each place once a quarter or at suitable intervals.

The forms used in various places for medical examinations for anglo-vernacular schools are more or less of the type which was published in the *Indian Medical Gazette* as early as

February 1923, and its standardization for each province is a matter of detail. The important point about the details of the form is that there should be uniformity in judging the defective conditions. The personal factor will be largely eliminated if the work is done for a number of years by the same person, who devotes himself entirely to the work, as already suggested. An annual conference of the members of the school medical service would be most helpful in the standardization of the methods and records of inspections.

The problem of the medical inspection of vernacular primary schools in towns stands on a different level. To leave it to the municipal committees to devise their own method of school medical work, as the vernacular education is their responsibility, amounts to an evasion of the problem. As only a small proportion of children of vernacular primary schools go on to higher education, their medical inspections should be of a modified form. There should be a six-monthly parade examination for the main defects of the eye, ear, nose, throat and skin of all children in a school and, to facilitate subsequent checking, the names of defective children only may be noted down in the register. The inculcation of health habits should be relied upon as the chief means of correcting the root causes of the school child's defects, and this is best done through the Junior Red Cross movement which has been popularized under the guidance of school teachers, designated counsellors, who receive a departmental recognition of their good services.

The practice of eight or ten simple health habits, *e.g.*, paring of nails, cleaning of teeth, daily bath, chewing of food, sleeping with the face uncovered, which are a child's own concern and for which the parent's intervention or assistance is not essential although advisable,³ is the most important feature of what is called the Health Game of the Junior Red Cross. A daily record of the practice of these habits is maintained by the child himself, and is checked by the counsellor, who at the end of the month, according to the marks scored, divides the children into three groups of good, fair and bad, and awards gold, silver and black tokens of appraisal, made at a very small cost by cutting out star-shaped pieces from paper of the required colour, and pastes them on a sheet of white paper against the names of the children in each class, the class record showing clearly how they have behaved from month to month. The counsellor will also arrange for the midday feeding of the children with sprouting gram specially prepared by soaking it in water for two days, the cost of which should be met by the municipal committee.

Medicine chests kept in vernacular primary schools have increased the incidence of headaches and 'tummy' aches, or resulted in a waste-age of quinine, and this unsupervised medication

cannot be too strongly condemned when municipal dispensaries and hospitals are available in the town. These municipalities should however have an assistant to the medical officer of health who should do the school inspections and be available for the 'dispensary' work at one of the municipal institutions, if medication work of school children is to be done. In any case the responsibility for medical inspections, if they are to be made uniformly effective, should rest with a whole-time agency when the volume of work demands it.

Ninety per cent of the total population of most provinces live in rural areas, and not even 5 per cent go on to higher education. The principle recommended for conducting medical inspections in vernacular schools of municipal areas should be applied to rural areas as well. It is however felt that with the provision of only a skeleton staff in districts, it would not be possible to expect the same degree of scrutiny as when the work is done by a separate agency. Nevertheless school medical work in rural areas is so mixed up with the other aspects of the district health work that the employment of a distinct agency for school work, even if the district board could afford it, would be found hardly desirable. If there is sufficient staff, let them divide the area for intensive work, and each one should intensify the school work in conjunction with his other responsibilities. Since the one or two qualified officers available for the district work at present cannot, even in most favourable conditions, reach a school oftener than once a year, every possible effort should be made with the assistance of educational officers to popularize the Junior Red Cross, and the maintenance of a small village medicine box in the larger schools situated far away from any medical aid should not be banned. Too much stress cannot be laid on the value of the Junior Red Cross in rural areas.

The various activities of the Junior Red Cross, which is the best means of securing the active interest of teachers, should form an integral part of school medical work for all kinds of educational institutions. The practical value of health education cannot be exaggerated and no amount of hygiene taught in schools can be effective if this aspect is ignored. Hygiene in spite of its importance is not treated as a major subject for examinations, as it is a practical subject for which didactic teaching is of no use without plenty of practice, and correct practice.

Summary

A system of school medical inspections for urban and rural areas based on the experience gained of the work is outlined, and the value of the Junior Red Cross as a means of educating children in health matters under the guidance of their teachers is stressed. The employment of a whole-time agency for the medical inspection of schools is urged.

A NOTE ON OCCUPATIONAL DERMATITIS IN THE JUTE INDUSTRY

By M. N. RAO

(Department of Biochemistry, Nutrition and Physiological Hygiene, All-India Institute of Hygiene and Public Health, Calcutta)

Introduction

INDIA practically holds a monopoly of raw jute production. Nearly ten million bales of raw jute, it is estimated, are produced in India. Some of the raw jute are exported to Britain and America, but nevertheless India contains more than half the total number of looms in the world. Jute cultivation is confined almost entirely to Bengal, Assam, Bihar, Orissa and to a small extent the United Provinces. The optimum conditions for jute cultivation, *viz.* high temperature, deep soil of fairly fine texture, rainfall of over 40 inches and a sufficient supply of clear

for spinning. The yarn is spun in various required types on to bobbins. The warp and weft yarns are separated and wound by the winding and beaming machines before being put on the loom. The woven cloth is made to go through the various machines, such as damping, calendering, lapping, cutting, beaming and sewing machines, before the finished product is obtained.

Dermatitis in the industry

In the out-patient department of any of the jute mills especially in winter, it is not uncommon to see at least one case in a day of a peculiar eruption on the skin of the forearms. On visiting the various sections of the factory one may also find that the workers in some of the sections are fairly exempt from this skin condition. Hence statistics of the various sections were taken with regard to the incidence of the disease.

Department	NUMBER OF CASES WITH DERMATITIS ON BOTH THE FOREARMS				Number of cases with dermatitis	Number of cases without dermatitis
	1 follicle	2 follicles	3 follicles	More than 3 follicles		
1. Batching-preparing ..	4	1	1	0	6	100
2. Finishing ..	13	3	1	0	17	100
3. Batching (after oiling) ..	11	10	2	2	25	100
4. Weaving ..	27	4	1	..	32	100
5. Spinning ..	25	19	9	4	57	100
TOTAL ..	80	37	14	6	137	500

retting water, being present in Bengal (Low, 1940), Bengal leads in jute cultivation and also in the jute industry. This jute industry, being different from other industries, presents its own peculiar problems.

While visiting various mills to study industrial hygiene, my attention was drawn to a papular eruption on the forearms, which was fairly common and has been diagnosed as 'phrynoderma'. As the eruption seemed to be different from phrynoderma, though resembling it in many aspects, it was thought worth while to study the aetiology of this dermatitis.

Flow sheet of the jute industry

Raw jute is brought from the fields to the mills. The jute of correct dimensions is 'selected' and put on the softening machines. The softening process is done by the liberal application of 'batching oil', a mixture of a special variety mineral oil and soap. The hard roots of the softened jute are cut off for use in coarser fabrics and the soft jute is weighed and put on the 'breaker cards' which comb the jute and form it into broad ribbons, 'slivers', and then on the 'finishing cards' to make finer ribbons. The slivers are then passed on to 'drawing' and 'roving' machines where the slivers are made into 'roves', or soft quarter-inch ropes suitable

In the other departments the incidence was very little, not even one case with dermatitis for every 100 persons without dermatitis being found. It is noticeable that the disease is fairly common in the spinning, weaving and batching sections.

Seasonal incidence

From the case sheets giving histories of seasonal incidence, it is seen that 12 per cent of the cases suffer from the disease in all the seasons of the year; 80 per cent of the cases give a history of the onset and recrudescence of dermatitis during the winter months—November to February—the condition gradually disappearing in the months of April and May. The remaining 8 per cent of the cases give a history of the onset of the disease in the summer months of May and June. It may be interesting to note at this stage that in and around Calcutta, where the jute mills are to a large extent situated, the mean daily temperature during the winter months of November to February is less than 75°F. (64° to 74°) and in the other months more than 75°F. (80° to 87°)—(Normand, 1939).

The onset

The part affected is not usually very hairy, and the eruption is preceded by a mild local

erythema. At first a small whitish 'comedo' appears either on the forearm or leg, of the size of a pin-head. Several usually appear at a time, but they are discrete and not necessarily in clusters (*vide* plate IV, p. 19) and fairly symmetrical. The acne-like eruption continues for a week, during which time the base of the eruption becomes pigmented and after which the 'pulp' can be easily removed leaving a small depressed area in its place. This depression, usually slightly pigmented, can be seen for a few seasons. Occasionally a few of these raised comedones remain as follicles with the pulp exsiccated. It is at this stage that they resemble very much the follicles of 'phrynoderma'. At no stage does the condition show any signs of inflammation. During the early erythematous stage, slight itching may be complained of, and at this stage it is liable to be secondarily infected. In none of the cases were there any signs of malignancy, nor was any case of such development revealed by enquiry from the workers and the medical staff.

Distribution

The commonest site of the eruption is the postero-lateral aspect of the forearm. The following table represents the number of the follicles in a unit area of the body surface in a series of 30 cases:—

Dorsum of the wrist including the lower thirds of the dorsum of the forearm	167
Elbow	90
Medial aspect of the thigh	85
Lateral gluteal region	67
Lateral aspect of the thigh	62
Lateral aspect of the leg	59
Bend of the knee	53
Posterior deltoid fold	37
Dorsum of the hand	32
Medial aspect of the leg	30
Face and neck	25
Antecubital fossa	20
Back	19
Lateral axillary fold	10
Abdomen	10
Dorsum of the foot	3
Palm	1
Foot	0

The histopathology

Epidermis.—There is marked superficial hyperkeratosis, without any signs of parakeratosis (imperfect cornification). The hyperkeratosis extends also into the pilosebaceous follicles where it can be seen as a plug of onion-shaped layers in the enlarged mouths of pilosebaceous follicle. The other layers of the epidermis are normal except that there appears to be an increase in the number of cells in the stratum granulosum and the basal layer (*vide* photomicrograph, plate IV, facing page 19).

Dermis.—Perifollicular infiltration is present, the predominating cells being mononuclear lymphoid cells. Young fibroblasts are also seen, indicating a localized subacute inflammation.

There are no changes seen in the sweat glands or the sebaceous glands.

Discussion

It may be recalled that the departments where the dermatitis is seen commonest are the spinning, weaving and batching departments. It is also rarely seen in the departments in which jute is handled before the batching oil is applied, as well as those departments which handle the finished product. Therefore the likelihood is that one of the two, the jute itself or the softening oil, may be the causative agent of the dermatitis. Moreover of the three departments where the dermatitis is most seen, it is in the spinning department that the oil that is soaked into the fibre is made to exude during the process of giving the spin to the fibre; whereas in the batching department the oil is taken up by the fresh raw jute, leaving little outside to come in contact with the skin of the workers. The idea that oil may cause the dermatitis is supported by the distribution of the lesions. In these departments the workers carry the jute on their forearms from one work place to another, and therefore the forearms are likely to be most affected by the contact with the oil. The low economic status and the unhygienic habits of the people lead to their factory clothes being changed only once or twice a week, and all the clothes are more or less plastered with the fine jute dust and the oil; naturally the skin that is covered by the loin cloth is liable to the deleterious effects of the oil.

The composition of this softening oil varies with the various mills but the main ingredients are a mineral oil, soft soap and other oils, such as castor oil, etc.; to elicit the aetiological agent of the dermatitis, a patch-test was done on a group of eight patients in one of the mills and on one of us. The mineral oil and the soap were tested without any dilution, and also the batching oil, *i.e.* the mixture of the two as actually used over the jute fibres (50 gallons of mineral oil in a mixture of 135½ gallons). The area selected for the test was the upper arm about the level of the insertion of the deltoid. There was no change in any of the areas where the batching oil and the soap were applied even after 72 hours, but in the case of the mineral oil, three of the cases, including one of us, showed an erythematous reaction during the third day. Further co-operation from the patients could not be obtained, but in the case of one of us the test was continued for two more days without the erythematous condition getting worse. The redness disappeared, however, during the 24 hours after removal. Judging from the results one is justified in concluding that the patch-test is positive for mineral oil, for a positive patch-test is one in which the irritant to which an existing eruption is presumed to be due should reproduce the initial features of the eruption (Tulipan and Glass, 1942), and erythema, as

already described, is one of the early symptoms of the jute dermatitis.

Differential diagnosis

1. *Alkali dermatitis*.—Other evidence also tends to substantiate the above presumption, because, though the oil is the constant primary ingredient in all the mills used, the pH of the final solution varies in various mills. Thus, in one of these, the pH of the batching oil used was 7.6 and in another, 9.6, but the disease is fairly common in both the mills. Thus, probably the alkalinity of the batching oil does not play an important part in causing the dermatitis though it may aggravate the condition. 'The skin reacts unfavourably to an excess of oil which is alkaline in reaction and mixed with fine abrasive particles' (Bridge). Moreover, alkaline dermatitis usually is associated with ulcers as can be seen in lime ulcers in hide unhairers and soda ash ulcers in chemical workers (Schwartz, 1936).

2. *Lubricating oil dermatitis*.—Dermatitis due to lubricating and other similar oils is supposed to be commonest in Germany and second commonest in England according to Legge (1934).

In mule spinners in the textile industry also, this condition was common and was investigated because of the possibility of development of cancer subsequently. Though oil dermatitis described by some workers (Hamilton, 1934) resembles the one described here, it seems to be different aetiological and clinically. Clinically, this condition is characterized by an acnoid infection of the hair follicles, which subsequently become dilated and coalesce as the surrounding corium becomes infiltrated with round cells (Ling, 1937). It seems that Purdon's *button d'huile* (Hope *et al.*, 1923), or oil acne, comes under this category.

It may be interesting to record some of the varieties of industrial dermatitis reported so far which resemble that in jute industry.

Silk throwster's dermatitis

Dermatitis under conditions similar to those of the jute dermatitis develops in the silk industry (Schwartz and Tulipan, 1934). Before silk winders put the skeins of silk on the winding rolls, they spread the skein by putting it over the hands and stretching it out. This brings the moist silk in forcible contact with the back of the hands where the dermatitis occurs, and from patch-tests done on affected cases it was found that most of the dermatitis was due to the solution used for the wetting of the weaving silk.

The wetting solution consisted of 10 per cent sulphonated olive oil, 1 per cent sulphonated coconut oil, potassium carbonate 0.7 per cent and anti-mildew consisting of 45 per cent sulphonated olive oil in water.

Of these various components it was found by the help of differential patch-tests that, although the anti-mildew was irritating to a few

of the girls, sensitivity to the olive oil soap was the chief cause of dermatitis.

Dermatitis in safety glass manufacture (Schwartz, 1939)

'Safety glass for automobiles is manufactured by gluing two panes of glass to a thin sheet of transparent resin (cellulose acetate or vinyl resin) inserted between them. This is then passed through a series of rolls under pressure. Throughout this process the glass is sprayed with diethylene glycol. When the glass emerges from the press machines, it is placed in an autoclave containing hot petroleum oil to 'cure' or to complete the 'cementing process'. Folliculitis with small pustules involving the hair follicles occurred in the workers who are employed in placing the glass in the autoclaves and removing it after 'curing'. The oil consisted of a light straw-coloured petroleum oil and the patch-test on the patients was positive with the curing oil and not with diethylene glycol.

Dermatitis in the linseed oil industry (Schwartz, 1934)

One of the causes of dermatitis in the industry of the manufacture of linseed oil is due to hypersensitivity to linseed oil and perhaps to the contaminants—mustard and rape oils. The dermatitis may take many forms, but the most common are folliculitis, acne and pustules.

Dermatitis in the glass-wool industry (Schwartz, 1939)

In the glass-wool industry also, dermatitis is reported as due to the sharp particles of glass (slugs) and the use of an alkaline oily solution to make the threads adhere to each other.

Conclusions

Thus, jute dermatitis can be classified under the heading of occupational dermatosis as it conforms to the definition by the committee on industrial dermatosis of the section on dermatology and syphilology of the American Medical Association—'A pathological condition of the skin, for which occupational exposure can be shown to be a major, causal or contributory factor' (Lane, 1942). The condition is directly attributable to the high boiling point (300°C.) of mineral oil used in this industry, aggravated probably by the hyperkeratosis of the skin and is not due to the oil preventing the skin from exfoliation, the condition being brought about only by mechanical blocking of the sebaceous gland orifices by plugs of the unexfoliated stratum corneum (Curgel and Acton, 1924). The hyperkeratosis seems to be present even beyond the follicles and it is probably secondary to the mild keratolytic action of the alkali present.

Summary

Occupational dermatitis in the jute industry is described and its aetiology discussed. The

mineral oil used in softening the jute appears to be the causative factor.

Acknowledgments

My thanks are due to the management of the Sir Adamjee Jute Mills, Belur, and Union Jute Mills, North Calcutta, for providing me ample facilities to carry on the investigation. Dr. Z. Ahmed was of great help in securing the material.

My thanks are due to Dr. B. P. Trivedi for confirming the histological findings.

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Reviews

SURGICAL PRACTICE OF THE LAHEY CLINIC, BOSTON, MASSACHUSETTS. 1942. W. B. Saunders Company, Philadelphia and London. Pp. xi plus 897, with 376 illustrations. Price, \$10.00. London Price, 50s.

THERE is a definite demand by general practitioners and specialists for collected papers of the well-known American clinics. Perhaps the general practitioner will not bother a great deal about technique and surgical methods but he will be vitally interested in recent diagnostic measures and results. With the ever-widening scope of the art of surgery, every attempt is made at standardization. Dr. Lahey may be right in saying that 'as we have standardized operations we have widened operability, decreased mortality and improved end results'. These words may be profitably remembered.

Although this volume may appear to be a collection of recent publications by members of the Lahey Clinic, closer scrutiny will show that the subjects treated here cover the whole range of major surgery. The first section deals with diseases of the thyroid gland,

comprising intrathoracic goitre, malignancy and hyperthyroidism complicated by other conditions.

The next section is devoted to the œsophagus and lungs and in particular to œsophageal diverticula, empyema, and lobectomy for bronchiectasis. The section on the breast deals with the problem of carcinoma. It is interesting to note that pre-operative roentgen therapy is not practised in this clinic; it is instituted usually ten days or two weeks after operation, and consists of the administration of 2,400 R units over three areas, viz, the supra-clavicular, axillary and breast areas. The section on the alimentary tract is fairly comprehensive. After varied experience with all the types of gastric resection, the Hofmeister type of subtotal gastrectomy with ante-colic anastomosis is recommended. The surgery of the biliary tract, particularly in such conditions as stone and stricture of the common and hepatic ducts, is discussed with great care. The section on diseases of the large intestine includes several important chapters. The 'Lahey resection' for cancer of the rectum is worthy of careful study. It is a two-stage abdomino-perineal resection and is used in 60 per cent of cases. It is claimed that the resection has 'the same degree of radicality' as the one-stage operation. Spinal anaesthesia is employed in all cases.

The section on gynaecology deals with the difficult subjects of dysmenorrhœa and vesico-vaginal fistula. During recent years the treatment of carcinoma of the cervix uteri has gradually become a problem for the radiologist. Treatment by irradiation is recommended for all cases except for epidermoid carcinomas of grade I stage I. Under urology, the technique of transurethral prostatectomy is discussed fully. There is a large section devoted to orthopaedic surgery; the article on sciatic pain of unknown origin will be found of interest. Surgery of the nervous system is often a closed book to the general practitioner who will find here no less than twelve interesting chapters for perusal. Surgical treatment of hypertension is a recent innovation comprising a surgical interruption of sympathetic impulses to the greater splanchnic region. It is fitting that the closing section of the book is devoted to the subject of anaesthesia. Some recent measures include the clinical use of cyclopropane, helium and fractional spinal anaesthesia.

We have read this volume with pleasure and profit and can commend it to our colleagues. The printing, get-up and illustrations are excellent. A useful index is appended.

P. N. R.

FRACTURES AND DISLOCATIONS.—By Kenneth M. Lewis, B.S., M.D., F.A.C.S. 1941. Oxford University Press, London. Pp. viii plus 217. Price, 10s. 6d. Obtainable from Oxford University Press, Bombay and Calcutta

THIS book gives a fairly comprehensive outline of the pathology, diagnosis and treatment of fractures and dislocations. The subject-matter is presented in tabular form under different headings.

It is easy to obtain information on any given fracture quickly, but the book suffers by comparison with other books because it has no diagrams and x-ray pictures.

The author's views in general are in agreement with the modern teaching on fractures. He is a keen supporter of the use of gravity, as for example in treating fracture dislocations of the cervical spine or in reducing difficult dislocations of the shoulder. Many surgeons, however, would not agree with him that removal of both fragments of the carpal scaphoid in late cases of fracture usually gives a painless wrist with complete range of motion. It is difficult to agree with the author's claim in the preface, that this book should be used to supplement the larger works on fractures, but it should prove extremely useful to medical students especially just before their final examinations, and also to the busy practitioner who wishes to refresh his memory quickly on any particular fracture.

H. G. N. C.

AIDS TO SURGICAL ANATOMY.—By J. S. Baxter, M.B., M.Sc., F.R.C.S.I. Second Edition. 1942. Baillière, Tindall and Cox, London. Pp. vii plus 193. Illustrated. Price, 4s. 6d.

This is an excellent little book. The author has contrived to crowd a large amount of information into comparatively few pages.

Like all books of this type it has to be read carefully in order to derive the maximum benefit from it, but the reader will find a number of very useful points to be learned, and also that certain anatomical regions, which have always been traditionally difficult to explain, such as the cervical fascia, the peritoneum and the pelvic fascia, are dealt with in a practical manner and with refreshing brevity.

All medical students will be amply repaid for reading this book before taking any surgical examination.

H. G. N. C.

ABDOMINAL SURGERY.—By John E. Hammett, M.D., F.A.C.S. 1941. Oxford University Press, London. Pp. xii plus 356. Price, 10s. 6d. Obtainable from Oxford University Press, Bombay and Calcutta.

It would surely be impossible to compress more information into a small space, than has been accomplished in the 336 pages of this book.

The writer clearly states in his preface that the volume is intended for the student; for the pre-graduate stage, it has undoubted value for the final stages of revision before an examination. This would appear to be the limit of its usefulness, for the earlier phases of study cannot be served by such synoptic tabulation; in the post-graduate stage, the junior surgeon demands a wider discussion of the broader aspects of his art.

Most of the sections of the book are packed with a wealth of detail, being supported by a bibliography of undoubted value. Most are spoiled by the elementary nature of preliminary anatomical and physiological subsections. For instance, it should scarcely be necessary to record that the stomach has two orifices, two curvatures and two surfaces before passing to the intricacies of gastro-duodenostomy and gastrectomy, or that the small intestine has a mesentery before describing the four stages of regional ileitis.

Practical instructional details are often impoverished by the absence of illustrations which would be well accommodated on many of the superfluous blanks which have been included for notes.

'*Multum in Parvo*' might well be an alternative title for this work.

ENDOCRINOLOGY. CLINICAL APPLICATION AND TREATMENT.—By August A. Werner, M.D., F.A.C.P. Second Edition. 1942. Henry Kimpton, London. Pp. 924. Illustrated with 327 engravings and a coloured plate. Price, 45s.

There comes a time in the development of all new branches of medicine when the great accumulation of experimental and clinical material requires collation and synthesis.

This time has come for the subject of the ductless glands and the want has nowhere been better filled than by Dr. Werner in his book upon endocrinology.

The opening chapters upon the autonomic nervous system and the action upon it of drugs and of the internal secretions are well done, though we think insufficient reference has been made to the important work of Dale.

The brief and well-illustrated introductions upon the anatomy and physiology of each gland and the short histories of the work done upon them are clear and valuable.

The illustrations, to which the subject lends itself, only less well than does dermatology, are well chosen and numerous.

This book is to be commended and recommended.

C. S.

THE MODERN TREATMENT OF VENEREAL DISEASES.—By E. T. Burko, D.S.O., M.B., Ch.B. (Glas.). 1942. John Bale Medical Publications Limited, London. Pp. 105. Illustrated. Price, 12s. 6d.

This clear exposition of the subject is a pleasure to read and the pleasure is enhanced by the clear print, wide margins, and fine paper.

There is much for praise and little for criticism beyond half a dozen errors in spelling the names of drugs, which no doubt will be corrected in the next edition.

We don't like 'ampoule' used as a verb as it is on page 13.

The value of T.A.B. vaccine and of the sulphonamides in the treatment of paradenitis might well be referred to; and it is open to question whether 'every pregnant woman should, as soon as pregnancy is diagnosed, have a Wassermann and Kahn test done upon her blood serum'.

It is satisfactory to see that Colonel Burke found doses such as 4.5 grammes a day of sulphonamide sufficient in the treatment of gonorrhoea and not the 17 grammes a day dosage which we have seen produce anuria from the blocking of renal tubules. This serious complication of sulphonamide therapy has escaped mention.

C. S.

A HANDBOOK OF MODERN PHYSIOLOGY.—By R. K. Pal, M.Sc., M.B. (Cal.), D.Sc., M.R.C.P. (Edin.), F.R.S.E., and A. Chakravarty, B.Sc., M.B. (Cal.), F.R.C.P. (Edin.), F.R.S.E. Second Edition. 1942. The Book Company, Limited, Calcutta. Pp. xvi plus 780. Illustrated. Price, Rs. 12-8.

The fact that the second edition has been called for is a sufficient proof of the usefulness of the book. The present edition has been increased by about 184 pages and a number of new illustrations have been included. The authors have given in a concise form the up-to-date ideas that the student of physiology should know. This book has removed a long-felt want. The portions dealing with biochemistry, vitamins, nutrition have been well revised. The sections on the nervous system and the endocrine organs have been extensively rewritten. The portions on applied physiology will be very useful to the modern student of physiology. The book will be of great help to the students preparing for their 1st M.B. examination in physiology. There are a fair number of printing mistakes and also a few minor omissions. On the whole the authors deserve credit for bringing out the second edition in such difficult times. It is hoped that this edition will meet with the same reception as the first one.

P. D.

EDINBURGH POST-GRADUATE LECTURES IN MEDICINE. VOLUME II. 1940-41.—By Various authors. Published for the Honyman Gillespie Trust by Oliver and Boyd, Edinburgh. Pp. xi plus 540. Illustrated. Price, 12s. 6d.

THE thirty-three lectures which comprise this volume were organized under a grant from the Trustees of the late Mrs. Honyman Gillespie and delivered in the Edinburgh Royal Infirmary during 1940-41. The range of the subjects is wide and varied and reflects credit on the Committee responsible for the lectures. They include hypertension, effort syndrome, blood examination, dietetic treatment of gastro-intestinal disease, wound infection and shock, burns, anaesthesia, venereal diseases, pelvic contraction, significance of fear, etc. The book opens with a thought-provoking article by Prof. Crew on the 'Contribution of Genetics to Reconstructive Medicine' in which he outlines how the science of genetics can be applied to human affairs as in the case of animals, and the genetic constitution of the human population altered according to a chosen ideal. Professor McDowall discusses the 'physiological approach to medical problems' and shows how it may assist the prevention, diagnosis and treatment of disease. Dr. Batchelor gives much practical information

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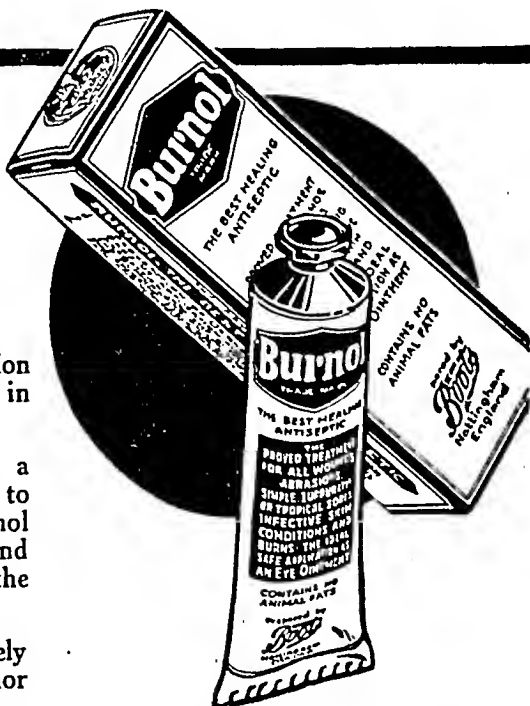
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about the treatment of syphilis and gonorrhoea and rightly lays stress on the essential difference between the treatment indications and requirements of the early case and those of the late old-standing infections. Colonel Stewart Middleton's article 'The Work of a Regimental Medical Officer' will prove informative and useful to many of our young doctors who have joined the army medical services. These are only some of the good features in the book and we recommend it to our readers and ask them to keep a copy by their bedside. They will find it delightful to read as well as stimulating.

R. N. C.

THE PREMATURE INFANT: ITS MEDICAL AND NURSING CARE.—By Julius H. Hess, M.D., and Evelyn C. Lundeen, R.N. 1941. J. B. Lippincott Company, Philadelphia and London. Pp. xii plus 309, with 74 illustrations. Price, 21s.

This book is well written to suit nurses, students and practitioners. In India there are very few establishments for the care of premature infants but this book will be a valuable guide to such nurseries. The chapter on feeding and clothing is illustrated in detail and is easily intelligible even to the lay public. The book will be an asset to the library of all medical and nursing institutions in India.

HEALTH BULLETIN NO. 31. THE HOUSE-FREQUENTING FLIES, THEIR RELATION TO DISEASE AND THEIR CONTROL.—By I. M. Puri, M.Sc. (Punjab), Ph.D. (Cantab.), F.R.E.S. 1942. Printed by The Manager, Government of India Press, Simla. Pp. 34. Illustrated. Price, As. 6 or 7d.

A POPULAR lecture entitled *Mosquitoes and Houseflies* by Major F. W. Cragg, I.M.S., was published in the Health Bulletin series in 1924. This is now out of print. The portion dealing with mosquitoes has since been treated independently in Health Bulletin No. 5. A *Lecture on Flies*, also by Major Cragg, was issued as a separate health bulletin in the same year. This too is now out of print and the publication of a new bulletin dealing with this subject has thus become necessary. In the following pages an attempt has been made to present the salient facts regarding houseflies and their control by up-to-date methods in the simplest manner possible.

'The name *flies* includes a large number of two-winged insects belonging to many different families varying widely both in appearance and habits. This bulletin is mainly concerned with those flies which are commonly met with in dwelling houses in intimate contact with man, and which are important from the public health standpoint.'

'Of the flies met with in dwelling places, the housefly is by far the most widely distributed. A number of useful books dealing with this insect, its relation to disease and its control have been published, but most of them are now somewhat out of date.'

The information collected in this bulletin will be very useful to the medical profession, and to the general public, especially those engaged in public health activities.

MEDICAL RESEARCH COUNCIL. EMERGENCY REPORT NO. 3. 'THE PERSONAL FACTOR IN ACCIDENTS.' 1942. Pp. 19. Printed and Published by His Majesty's Stationery Office, London. Price, 4d.

'The importance of efforts to lessen the number of accidents on the roads and in industry hardly needs emphasis, and the following pages indicate the personal factors which need to be considered in this regard. The statistical establishment of "accident proneness" as an unfortunate characteristic of a section of mankind—and the finding that this is to some extent predictable by psychological tests—is due largely to original researches by former and present members of the Board's staff. Much remains to be done from the point of view of increasing the scope and efficiency of the tests, and the Board's investigators hope for opportunities to extend their researches, in respect of

some of the bigger industries under war conditions. Such studies of the personal factor in accidents should be an effective and powerful ancillary to the preventive and protective regulations of the Ministry of Labour and National Service, and to the valuable propaganda of the Royal Society for the Prevention of Accidents, now part of the Ministry's organization. Safety regulations and propaganda necessarily relate to the conditions and dangers to which groups of operatives, or, it may be, the whole population, are exposed. The personal studies discussed in part II of this report deal, instead, with the particular case of the worker who—intrinsically and through no fault of his own—may be a danger to himself or others under certain conditions, and the chief object of the studies described is to find means of diagnosing his failing in advance so that he may be transferred to a safer type of work before his misfortune has manifested itself in a serious accident to himself or to others. The application of the psychological tests necessarily demands trained personnel, who may not always be available, but it is pointed out that the accident-prone may often be identified by the simpler expedient of a careful system of accident records, since those who have many minor accidents also tend to have major ones. Suggestions as to how these records should be kept are given in the report; and if its publication stimulates interest in the matter and leads to a better system of industrial record-keeping in regard to accidents, and to the consequent transfer of those shown to be accident-prone to tasks involving a lesser degree of danger, it will represent a noteworthy step towards the solution of an urgent problem of to-day.'

Abstracts from Reports

THE ROSS INSTITUTE OF TROPICAL HYGIENE (INDIA BRANCH): REPORT OF THE COMMITTEE OF CONTROL FOR THE YEAR ENDED 31ST JULY, 1942

THE importance of improving the health of labour in this country cannot be over-emphasized. In this connection, the Ross Institute reflects credit on the management of the tea and other industries which support its work. This organization in India has now been functioning over a period of twelve years.

Dr. G. C. Ramsay, the principal of the India Branch, has, during the past year, visited several malarious areas occupied by troops. The branch has helped the war effort by providing trained surveyors. Other main activities included biological measures of mosquito control, such as flushing streams by sluicing methods or by growing hedges along the banks of the channels with the object of producing sufficient shade to prevent growth of grass and weeds. This aspect of antimalaria work is important at the present time because of the shortage of quinine, oils, etc.

ANNUAL REPORT OF THE SOUTH AFRICAN INSTITUTE FOR MEDICAL RESEARCH, JOHANNESBURG, FOR THE YEAR ENDED 31ST DECEMBER, 1941

War work.—War requirements have resulted in great expansions in all branches of the Institute's work. The Director, as honorary director of pathology in the department of defence, is in charge of a military detachment concerned with the training of Army laboratory personnel, and the equipment of military laboratories. The various costly investigations that have been or are being carried out on behalf of the Army are done by civilian members of the Institute's staff who have, in several instances, been specially appointed for the purpose. These investigations include:—

Synthesis of vitamins in the Union, using locally obtainable material; production of vaccines and sera not normally prepared at the Institute such as typhus, influenza and yellow fever vaccine, and gas gangrene

serum; preparation of fluid and dried human serum suitable for administration to men wounded in the field; anti-malaria and anti-yellow fever measures, such as the preparation and testing of mosquito repellents, and surveying the geographic distribution of mosquito vectors in the Union and neighbouring territories; manpower research.

Research.—It was possible for most departments to continue investigations on which they were previously engaged. The volume of this research was large.

Leprosy.—The use of N.A.C. antigen, prepared from a new acid-fast variety of tubercle bacilli, in the treatment of certain forms of leprosy proved so encouraging that it was decided to follow up this work with further experiments. The clinical and immunological investigations on the treatment of leprosy by means of diphtheria toxoid according to the method introduced by Dr. Collier, of Thailand, were carried out. The 100 patients developed high anti-diphtheritic immunity as the result of a prolonged course of injections, but they failed to confirm Dr. Collier's claim for this form of treatment.

Pneumonia.—Cases of pneumonia clinically resistant to sulphapyridine therapy continue to be encountered. The majority of these are found to be associated with a *Staphylococcus aureus* either as the sole infecting agent or together with a pneumococcus or other organism. A number of these pneumonia cases have been treated with sulphathiazole with bacteriological control in these laboratories. In certain instances the results were highly satisfactory. It is concluded that, for the present, sulphathiazole, particularly in conjunction with an autogenous staphylococcus vaccine, is the best method of treating such resistant cases.

Typhus.—Dr. D. Ordman undertook the large-scale preparation of vaccine for prophylaxis in the typhus group of diseases. Vaccines will in future be available against exanthematic and murine typhus as well as against tick-bite fever. The vaccines are being prepared by the Zinsser-Castaneda method involving the use of irradiated rodents including gerbils and also the yolk-sac method in which the rickettsiae for vaccine suspensions are harvested from the infected yolk-sacs of developing hens' eggs. The comparative immunizing value of the various vaccines is being investigated by protective and other tests and experiments are also being conducted to determine the most effective means of killing the rickettsiae without impairing their immunizing value.

Relapsing fever.—The results of an investigation into the distribution of the *Ornithodoros moubata* tick and the occurrence of relapsing fever in South Africa have been published.

Lymphogranuloma inguinale.—The demand for Frei antigen in the diagnosis of cases of lymphogranuloma inguinale has led to interesting work with the bubo pus taken from cases of this disease. A large amount of this antigen was prepared.

A disease resembling tick-bite fever in its reactions in guinea-pigs was isolated from the tick *Amblyomma hebraeum*. The ticks were collected on cattle found in the vicinity of the golf club at Lourenco Marques. The links of this golf club are notorious as a source of human tick-bite fever. Experiments to establish the identity of this strain are in progress.

Mycology.—A case of histoplasmosis, the first to be noted in Africa, has been investigated. The causal fungus, *Histoplasma capsulatum*, was isolated and successfully grown on artificial media and some animal experimental work has been carried out.

Routine work.—Diagnostic work expanded further during the year, the number of examinations and tests done being 274,101, an increase of 45,053 over that of the previous year.

Blood cultures from cases of suspected enteric fevers numbered 1,020. The following pathogens were isolated from 179 of these cultures:—

<i>B. typhosus</i>	150
<i>B. paratyphosus A</i>	14
<i>B. paratyphosus B</i>	14
<i>B. paratyphosus C</i>	1

From specimens of faeces and urine the following were isolated:—

	Faeces	Urine
<i>B. typhosus</i>	.. 16	18
<i>B. paratyphosus A</i>	.. 9	1
<i>B. paratyphosus B</i>	.. 3	0
<i>B. paratyphosus C</i>	.. 17	2

Widal agglutination test.—A total of 6,458 specimens were submitted to the Widal test. Positive reactions with *B. typhosus* 'H' and 'O' were given by 2,427; this figure includes those that gave in addition reactions with *B. paratyphosus A* and *B. paratyphosus B*, usually as the result of prophylactic inoculation. A number of bacteriologically proved cases of typhoid fever, however, gave some agglutination reaction with *B. paratyphosus A* without a history of previous inoculation. *B. paratyphosus C* was agglutinated to diagnostic titre with sera from thirty patients. The 'Vi' agglutination test was done on 6,479 specimens for the detection of typhoid carriers amongst persons handling food. Of these, 261 or 4 per cent gave a positive reaction. Most of these specimens came from a distance. It was not possible, therefore, to examine the reactors further as to the carrier state. Urine and faeces of fifteen positive reactors, examined on three successive days for *B. typhosus*, gave negative results. The serum of a native urinary carrier gave a positive 'Vi' agglutination test in dilutions up to one in eighty. His titre for 'O' was 1 in 200 and for 'H' 1 in 100. Tests done on different occasions showed that there was very little fluctuation in his 'Vi' agglutinin.

Typhoid complement fixation test.—Of 1,101 specimens submitted for the typhoid complement fixation test, 72 gave positive and 151 doubtful results.

Of 1,107 specimens examined by the Weil-Felix test, 138 gave positive reactions with *B. proteus* OX. 19 and 102 with *B. proteus* OX 2. Cross agglutination between these two types of *B. proteus* was common, while a number of specimens gave additional agglutination with *B. proteus*, ONK.

Of 873 specimens examined for the presence of agglutinins of *Br. melitensis* and *Br. abortus*, 26 specimens gave a positive diagnostic reaction. The serum of 1 patient who had a positive blood culture for *Br. abortus* showed a titre of 1 in 6,400 for this organism, and a titre of 1 in 200 for *Br. melitensis*.

Correspondence

QUININE AS A MALARIA PROPHYLACTIC

Sir,—At a meeting of the Royal Society of Tropical Medicine in London in 1925 (Yorke, 1925) at which the uses of quinine were being reviewed, the president remarked that the general position was hopeful 'save perhaps from the point of view of prophylactic quinine', and another doctor described this aspect of the subject as 'the eternal question', the implication being that it was one not yet settled.

This officially slams the door in the faces of those who have already made up their minds about the matter, one way or the other.

Struth, there are many diverse reports on the subject. For instance, there is one of an experiment by Field, Niven and Hodgkin (1937), cited by Napier (1938), the outcome of which was successful, and on the other hand there are the accounts of the Army experiments during the last War when half battalions at Salonika were given 'prophylactic' quinine while the other half had nothing and the results were negative.

Now the diversity in the results of such experiments can, it is submitted here, be explained, and the explanation leads to this conclusion, that if 'prophylactic' quinine be given to an immigrant and susceptible population it has no effect on the malaria-rate, but if it be given to a settled population in a malaria-endemic area it will to a certain extent succeed, not that it is advisable even here.

The whole thing hinges on the observations in Holland by Korteweg (Swellengrebel and de Buck, 1931 and 1932) that during the stage of 'Korteweg's initial

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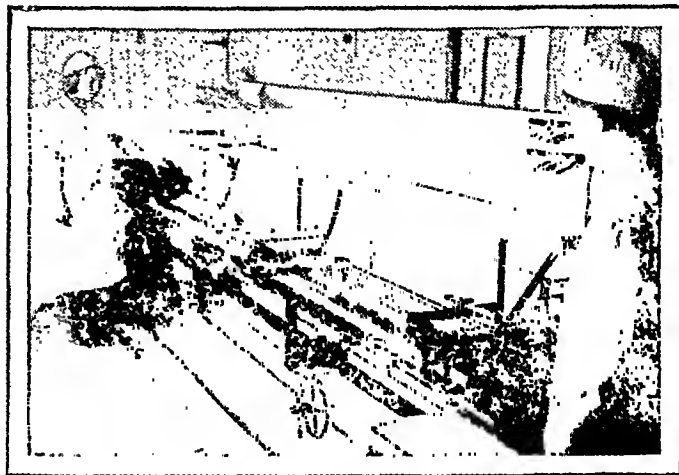
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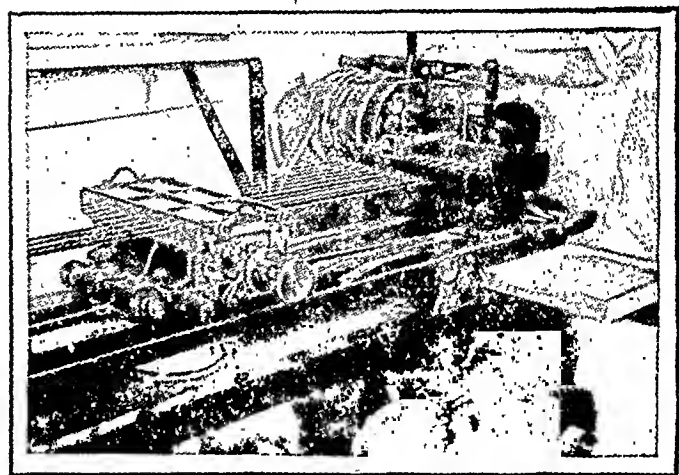
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The appointment is for five years in the first instance, with a salary of £1,200 per annum.

The appointment is a whole time one, and the Professor will normally be required to devote part of his time to the duties of a Surgeon at the Royal Eye Hospital and the remainder to research work at the Royal College of Surgeons. Further information will be given on request.

Applications should reach the Secretary of the Royal College of Surgeons on or before the 1st March, 1943, accompanied by a statement of qualifications and experience and the names of three persons to whom reference may be made.

KENNEDY CASSELS,
Secretary.

Applications by Cable to Royal College of Surgeons of England

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IMPORTANT NOTICE

DOWN BROS. LTD. regret to announce that owing to war conditions they are obliged to close down their Office and Showrooms at 16, Old Court House Street, Calcutta.

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They look forward to a continuation of the valued relations with their friends in the Indian Surgical world, which have existed for over fifty years.

fever' quinine has no action at all and on their explanation that it is only when there has been a certain initial systemic reaction that quinine can act as a parasiticide.

In other words, if quinine be given 'prophylactically' to a number of immigrants who have never had malaria, *e.g.*, to British soldiers, or to Tamil labour, no amount of the drug will prevent the primary manifestation of the fever, *viz.*, 'Korteweg's initial stage', and this will run its course even during the concurrent administration of the quinine. If then, however, when that initial stage be over, and when that putative systemic reaction has taken place, quinine be still continued, it will stop the fever *quâ* therapeutic agent. 'Prophylactic' quinine in such pure communities therefore would show no results, as it did for all practical purposes at Salonika, but the course given, if continued, would as stated show therapeutic results, which means that the cost of that proportion of the total used, that had been used 'prophylactically', had been wasted.

On the other hand, if 'prophylactic' quinine be given to a settled community in which malaria is endemic, some infection will have previously occurred in a certain proportion of the population, and this infection will have already had a run, and produced the systemic reaction which is essential for the successful action of quinine, so that in this section of the population prophylactic quinine would be instrumental in averting a reappearance of the same type of infection. The success achieved by Field, Niven and Hodgkin (1937) in the F.M.S. can be explained in this way. But even in such a community there will be other persons becoming infected with a type from which they have never suffered before and prophylactic quinine will not save them, as has been explained above.

But granted that in such communities prophylactic quinine does reduce the malaria-rate, it does not appear reasonable to spend vast sums of money for this purpose, when a mere fraction of that used 'prophylactically' will be sufficient to cure immediately the cases of fever that develop. One postulates a person in whom systemic reaction to a particular strain of infection has already taken place and the question arises: Is it better to dose him for perhaps months on end with five grains a day or wait till he develops fever, when a few grains of quinine (provided the infection is not of a newly-acquired type), will immediately cure him? Many an Assam Planter answers this question by habitually refusing to take 'prophylactic quinine', and only on the onset of malarial malaise taking 5 grains, with some hot toddy, which usually puts him right again.

Sometimes in both sorts of community, the susceptible immigrants and the settled endemicized community, the systemic reaction to an infection does not take place, presumably due to environmental conditions such as insufficient food, or excessive labour, and then in both communities prophylactic quinine will have no apparent effect.

Now what are the processes that take place during that 'systemic reaction' to the invasion of the parasite, and also pertinent to this question is, how does quinine act as a parasiticide?

With regard to the latter point, the potency of the drug outside the body appears to be at best very low, for if a quinine solution be added to defibrinated malaria-infected blood and the mixture incubated at body-temperature for 12 hours, it is infective on injection into a susceptible person, even should the strength of the quinine in the mixture be much greater than ever can occur in the human circulation after the drug is taken therapeutically. In spite of this Yorke and Macfie (1924) think that quinine when given therapeutically does 'kill off a large number of the parasites (the quinine perhaps first becoming altered by the body-cells, but against this hypothesis is the fact that the drug is eventually excreted from the body not in any altered condition), those dead parasites act as antigen and excite the formation, by the tissues, of immune-bodies, which then deal with the parasites surviving from the first action of the quinine.

Now when the writer was a medical student he was warned against facilely diagnosing two, or even more, causes for a disease, and it seems that in an analogous situation Yorke and Macfie have not followed this wise principle, they have invoked two processes by which the parasites are killed off:—

- (1) by the direct action of the quinine on the parasite,
- (2) by the production of immune-bodies, by the tissues, which also act on the parasite.

Now it may be argued against these hypothetical processes that (a) if the quinine starts off by killing large numbers of parasites, why should it not go on doing so until all the parasites are killed off, and (b) is the unnatural destruction by quinine of a preliminary batch of parasites necessarily antecedent to the production of immune-body? the answer to which is 'no', for the *natural* reaction of the tissues to the infection is quite sufficient to account for the provision of all the antigen required for the formation of immune-body: because natural reaction alone, as is well known, leads to the state of tolerance that one finds in the inhabitants of highly endemic areas. Yorke and Macfie's hypothesis appears therefore to be at its best superfluous.

How quinine acts is therefore a question still remaining to be answered. Accepting the evidence that quinine in circulation acting on an early infection has no parasitic action (as *in vitro*), and that it is 'only when the *natural* systemic reaction or reaction of the tissue-cells has taken place that the drug acts—further that the reaction of the tissue cells in itself usually suffices to cure a malarial-infection, but that the cure appears to be hastened by quinine, it appears likely that immune-bodies like amoceptors have been produced by the tissues that enable the quinine to be shackled on to the parasite, and until such amoceptors are produced no such action can take place.

Quinine, therefore, can be taken at any rate as a working hypothesis, to be useless either therapeutically or prophylactically, until the necessary tissue-reactions have occurred, and it then follows that to give it therapeutically before 'Korteweg's initial stage' is over is to waste the drug, and to give it prophylactically is even much more wasteful, because for all practical purposes the fever can be stopped, if it can be at all, by minimal doses when it breaks out. Of course the prerequisite tissue-reactions may not take place at all, and then quinine is completely useless and the only measures of any benefit are rest, good food, and so on.

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C. STRICKLAND, M.A., M.D.

CARMICHAEL HOSPITAL FOR
 TROPICAL DISEASES,
 CENTRAL AVENUE, CALCUTTA,
 2nd October, 1942.

[Note.—We are not in agreement with the writer's conclusions; they are also opposed to those of most malarialogists of the present day. The Committee of the League of Nations Health Organization which was responsible for the Fourth Report were fully aware of the work of Swellengrebel and his colleagues.—EDITOR, *I. M. G.*]

TREATMENT OF NAGA SORE

SIR,—Since 1930 I have had occasion to treat numerous cases of Naga sore, and the routine treatment of the Naga sore with the strongest antiseptics, such as carbolic acid, has met with failure in my hands. The bacteriology of the disease led me to think of spirochaetocidal treatment with N.A.B. As the germs

grow and multiply in the ulcer itself, local treatment of the ulcer with N.A.B. is the method I adopted. To my great satisfaction the treatment proved to be quite successful. To me it seems to be a specific drug since it healed all the ulcers within an unusually short time. The solution of N.A.B. used by me for the treatment of Naga sore is given below :—

R N.A.B. 0.30 gramme

Double distilled water 1 ounce.

I simply applied gauze soaked with the above lotion and dressed it twice a day. Complete cure within a fortnight is always seen.

MOHAMAD MOHIUDDIN,
L.M.P., L.T.M.,
Medical Officer.

MENERGANJ DISPENSARY,
DISTRICT PURNIA, BIHAR,
11th November, 1942.

IMPORT AND SUPPLY OF MEDICAL PREPARATIONS

Sir,—I am writing this to you on behalf of one of the most representative trade associations in this country whose members are concerned in the distribution of all kinds of drugs, chemicals and pharmaceutical preparations which are imported into India from the United Kingdom and the United States of America which are the only sources of supply for the Indian market under the present circumstances of war.

For some time past on account of the frequent shortages of many of the essential medicinal supplies, our member firms, who have established such long and cordial connections with the medical profession, some of them for over half a century, are coming in for a great deal of unpleasantness with their medical friends. Whilst my committee is sure our medical friends do appreciate that a number of difficulties confront our member firms these days in the matter of obtaining adequate supplies of drugs and medicines, it occurs to them that many physicians may not be conversant with all the factors responsible. Under the circumstances, my committee feel that in addition to expressing regrets on behalf of our members for not being able to take care of all the needs of the medical profession, we owe something in the nature of an explanation for the present unsatisfactory stock situation.

For your information, therefore, I enumerate below some of the chief causes responsible for the shortages of stocks which from time to time occur :—

1. Total prohibition of export of many drugs, medicines, etc., from England and America.
2. Restrictions on imports into India.
3. Delays which occur in the issuing of licences by the authorities.
4. Damage at points of shipment due to enemy action.
5. Loss of shipments due to enemy action.
6. Difficulties experienced by our laboratories in obtaining shipping space.
7. Length of time shipments are in transit.
8. Steamers being diverted and cargoes being off-loaded at other ports in India.
9. Shipments arriving in damaged condition.
10. Difficulty in obtaining rail-freight space in India and refusal on the part of railway authorities to grant priorities to medical goods, with the result that cargoes often remain stored in ports from which general distribution cannot be satisfactorily effected.
11. Manufacturing difficulties in England and America as regards obtaining sufficient supplies of raw materials, shortage of skilled labour, restrictions and embargoes on the use of certain raw materials, and shortages of finishing materials such as bottles, tins, vials, caps, etc.
12. Greatly increased demand to-day for English and American goods caused through the elimination of Continental competition and the influx into India of British and American fighting forces, also evacuees from countries now in occupation of the enemy.

The above no doubt will assist you in understanding the present position and my committee therefore express the hope that your association will appreciate that our member firms are doing the very best they possibly can under extremely difficult circumstances, to discharge their responsibilities to the medical profession and to their patients.

The aim is to distribute all supplies they receive as evenly and to as many of their patrons as possible, and this explains the necessity for what may appear to be drastic rationing on their part when small supplies become available from time to time. In this connection the Medical Profession will also appreciate the fact that despite only limited stocks available for distribution, the main distributors have not put up prices beyond legitimate limits, and are in no way responsible for the unprecedented speculative trend of the present-day drug market.

In placing the above facts before you, my committee would particularly draw your attention to the dilatory methods adopted by Government in issuing Import Licences which has resulted in the holding up of stocks which are ready for shipment from the United Kingdom and the U.S.A. My committee therefore wishes that the leading Medical Associations should use their influence in persuading the principal authorities concerned in Import Trade Control, namely, The Director-General, Indian Medical Service, and the Secretary to the Government of India, Department of Commerce, to facilitate an adequate supply of at least essential medicines which are required for the civil population.

I might also request that the situation in regard to import and supply of medical preparations as outlined above be brought home to each and every member of the profession. This may best be done by publication of this information in your esteemed *Indian Medical Gazette*, which favour I trust you will kindly grant.

for and on behalf of
*The Pharmaceutical and Allied
Manufacturers' and Distributors'
Association Limited,
Honorary Secretary.*

C/O KEMP AND COMPANY,
LIMITED,

CHARNI ROAD, BOMBAY,
28th November, 1942.

LORD LISTER AND THE TREATMENT OF WAR WOUNDS

Sir,—Genius is the grip upon first principles. Surprise, therefore, is not awakened, when the modern methods of treating war wounds throw a fresh light upon the genius of the greatest of surgeons and a man with every element of genius, Lord Lister.

Lister won his first success with his antiseptic system in 1868 and in 1870 the Franco-German war broke out. Preceding this war there had been the Crimean war, in which at Scutari in February 1854 the hospital deaths had been at the rate of 415 per cent per annum, so that, at such a rate, in twelve months the whole wounded and sick population of the hospitals would have perished four times. Lister was appalled by such results and, if possible to prevent their repetition, at the war's outbreak in 1870 he published a pamphlet giving a simple means of antiseptic treatment 'applicable to wounded soldiers in the present war'.

The pamphlet consisted of four pages and the following is a condensation of it: After dead matter had been removed, the wound was washed out with carbolic lotion and bleeding arteries were secured by antiseptic ligatures. The wound was then covered with a slip of oiled silk smeared with carbolic oil, then with a piece of lint or rag soaked in the oil, then a piece of gutta serena tissue overlapping the lint, once more a piece of lint or rag or towel, wrung out in the oil and the whole bandaged onto the wound. As blood soaked into the dressing, wrote Lister, the outer layer of lint, rag or towel should be removed, squeezed out and wrung out afresh in the oil. When the discharge ceased, damping of the outer layer with the oil every two days should be sufficient.

BOVRIL AS AN AID TO NUTRITION

Physiological facts disclosed by recent experiments

In many illnesses, when gastric secretion is impaired and is deficient in hydrochloric acid, Bovril corrects this condition by restoring the normal volume and activity of the gastric juice, thus aiding the peptic digestion and absorption of protein foods.

In 1911, the late Professor Thompson, of Dublin, established that Bovril had the power of ministering to nutrition by the assistance it gave to the assimilation of other foods. Recently a remarkable series of experiments has been conducted at an English University. A group of medical students volunteered to undergo the unpleasant experience of allowing the passage of an œsophageal tube into the stomach so that accurate studies might be made of the effect of certain beef preparations. One of the substances investigated was Bovril.

As a result of these experiments (described in detail in the *British Medical Journal* of August 28th, 1937) Bovril

emerged as 'the most effective stimulant.' Briefly, it was proved that Bovril increased the supply of gastric juices where there was a deficiency and restored it to normal. It is an accepted medical fact that people of sedentary habits generally suffer from a lowering of the essential gastric activity; Bovril rectifies this and, by facilitating the digestion of proteins, enables full nourishment to be gained.

Everyone, therefore, who is run down through strain or illness, or who feels in need of extra strength to cope with the demands of modern life, should take a cup of hot Bovril daily. It is a delicious and stimulating way of keeping fit and strong.

BOVRIL

ASSISTS ASSIMILATION

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*Dioxy-diamino-arseno-benzol,
N: N-Methylene sodium sulphite*

Sulpharsphenamine B. P.

A potent organic compound of arsenic of low toxicity specially intended for intramuscular use in all stages of syphilis.

May also be used intravenously

Every batch is tested chemically and biologically

Supplies :

0.075 gm., 0.15 gm., 0.30 gm., 0.45 gm. and 0.60 gm.

BENGAL CHEMICAL AND PHARMACEUTICAL WORKS, LD.
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**EMERGENCY
COMMISSION
OFFICERS FOR THE I.M.S.**

As a war-time measure the Government of India have decided to admit to the Emergency Cadre of the Indian Medical Service, Indian Medical Practitioners holding the M.B., B.S. degrees of the Mysore and Osmania Universities.

Candidates should ordinarily be below 45 years of age and fit for active military service.

APPLICATIONS with necessary documents should be made to the Surgeon General or Inspector General of Civil Hospitals of Provinces or to the Residency Surgeons. Bangalore and Hyderabad, or to the Director General, Indian Medical Service, New Delhi.

The inner dressing was not to be removed at all. The pain of its disturbance was to be avoided. After the initial treatment, only the outer layer, separated from the wound by the gutta percha tissue, was to be dealt with by the dresser. *The wound was, therefore, to be kept in a state of rest and its healing left to the healing power of nature.*

So, within two years of his first success with the antiseptic system, Lister applied the system to the wounds of war upon a basis of initial cleansing and leaving the wound for the vital forces to do their work of recuperation. His trust in his system did not unbalance his trust in the healing power of nature. 'Of all those who use antiseptics in surgery', he said at Edinburgh in 1870, 'I suspect that I apply the least to the wound. After the first dressing, the object which I always aim at is to have the material in contact with the exposed tissues as close as possible to the perfectly bland and neutral character of the healthy tissues'.

It is, then, of absorbing interest and instruction to find the first principles, which Lister as genius necessarily followed, are those which are inspiring much of the treatment of war wounds at the present day, seventy years after Lister published his pamphlet.

G. T. WRENCH, M.D. (Lond.).

(Author of *Lord Lister, His Life and Work*. 1913.)

VICTORIA ROAD, KARACHI,
SIND,
23rd September, 1942.

INFLUENCE OF ANTI-ANÆMIC TREATMENT ON THE GASTRIC FUNCTION IN HOOKWORM DISEASE

SIR,—Heilig and Visweswar's paper in your July number seems to me to involve some fallacies.

It is rather strange that they should have been content with raising the hæmoglobin to a mere 40 per cent and with drawing conclusions at this very low level on the mutual relationship between hæmoglobin levels and/or hookworm infection and gastric acidity. Incidentally we in the General Hospital here are struck with the very poor rate of hæmoglobin rise in Heilig's series, three to four weeks for a rise of 20 per cent at the very low initial level of 20 per cent hæmoglobin. We have sometimes been surprised at our exceeding Witt's (*Lancet*, 1936, i, 1) maximum rate of 2 per cent rise per day at low levels. We were previously using as a routine 30 gr., *t.d.*, of iron and ammonium citrate. We now use alternatively 3 gr., *t.d.*, of ferrous sulphate in solution. Heilig has been using Blaud's pill.

Heilig and his co-worker have brushed aside McRobert's figure of 1940 on the ground that they do not give the acid-titration figures. The fact remains that out of one hundred cases of anæmia reported in McRobert's paper no less than seventy-seven were uncomplicated hookworm anæmias, that twenty-seven of these were achlorhydric on admission, that in eleven out of these twenty-seven achlorhydric hookworm anæmias the achlorhydria was histamine-fast in seven, and that out of these seven initially histamine-fast achlorhydrics three continued to be histamine-fast, one secreted free acid without histamine and three with histamine, at the time of discharge with the full normal complement of hæmoglobin.

McRobert's paper was a bare factual summary. But it illustrates very well the point that I wish to emphasize that in the present state of incomplete knowledge, too much diagnostic and prognostic importance should not be attached to fractional gastric analysis. Apperly, Alvarez and Eugene Foldes on the one hand and Hurst and Napier on the other have in the correspondence columns of the *Lancet* (1936, i) brought out the possibilities of mutual cause and effect relationship of gastric acidity and blood count. It is unwise to dogmatize from one's own set of cases. Achlorhydria admittedly plays a causal rôle in the development of some iron-deficiency anæmias as it does in association with Castle's intrinsic factor in pernicious

anæmia and without in some nutritional megalocytic anæmias. This achlorhydria may be permanent or temporary, histamine-fast or not. That is all that can be said at present. The dosage of iron in clinical practice is and has to be so large that the presence or absence of acid secretion in the stomach does not appear to matter.

The rôle of the hookworm in causing achlorhydria cannot be definitely decided unless one deworms the infested patient before raising the hæmoglobin to fairly high levels and notes the effect of deworming on gastric acidity in a large series of cases. I have recently seen four or five cases of marked hyperchlorhydria in severe hookworm anæmia. I do not consider myself justified in jumping to the conclusion that hookworm causes hyperchlorhydria any more than it does achlorhydria.

S. K. SUNDARAM, B.A., M.D.

GENERAL HOSPITAL,
MADRAS,
13th August, 1942.

Service Notes

APPOINTMENTS AND TRANSFERS

LIEUTENANT-COLONEL F. H. WHYTE is appointed Civil Surgeon, New Delhi, with effect from the afternoon of the 19th October, 1942.

Lieutenant-Colonel L. A. P. Anderson, I.M.S. (Retired), is appointed Officer on Special Duty in the office of the Director-General, Indian Medical Service, with effect from the 26th October, 1942.

Lieutenant-Colonel A. H. Harty, C.I.E., whose services have been placed at the disposal of this Government assumed charge of the office of Inspector-General of Civil Hospital, C. P. and Berar, on the afternoon of 19th November, 1942.

LAND FORCES

To be Lieutenants

Ernest Burford Weeks. Dated 17th August, 1942.

James Wallace Lusk. Dated 7th October, 1942.

(Miss) Creina Shepherd. Dated 2nd September, 1942.

INDIAN LAND FORCES

(Emergency Commissions)

To be Lieutenants

(Mrs.) Gladys Connor. Dated 1st August, 1942.

(Miss) Putli D. Nanavatty. Dated 21st August, 1942.

(Miss) Gurbaksh Kaur Dhariwal. Dated 29th August, 1942.

William Henry Collins. Dated 2nd September, 1942.

George Edwin Aling. Dated 29th September, 1942.

Mahankali Krishnamurthi. Dated 1st October, 1942.

2nd October, 1942

Aswini Kumar Choudhuri.

Khodadad Muncherji Fozdar.

John Vincent Nazareth.

Bhola Nath Roy.

Ramchandra Dattatraya Marathe.

Cherukat Padmanabhn Nair.

Vickramasingapuram Namasivayam Ambalavanan.

Pradyot Kumar Basu.

Meethan Bhanu.

Paramban Kunimal Chandrasekharan.

Ambrose Jeyaraj Vedanayagam.

Alagala David.

Cottur Muthuswamy Sundarajan.

Mailachikal Jamaludin.

Chalavadi Venkateswarlu.

Namburar Gopalanaidu Kondaswamy.

Arun Kumar Basu.

Nironjan Chaudhuri.

Amal Kumar Das Gupta.

Baloram Mukerjee.

Balekudru Gururaj Achar.

Thomas Harcourt Emmanuel Henry Gnanaiya.

Andrew Peters.

Adiraju Gopala Moorthi.

Nirendra Narayan Das Gupta.

Ram Charn Singh Sandhu.
 Tinnevely Sundarosan Ganapathi.
 Guruprasanna Bhattacharjee.
 Kartick Chandra Das.
 Romendra Nath Chowdhury.
 Parayil Madhavan.

3rd October, 1942

Madurapakkam Doraiswami Ramamoorthy Naidu.
 Vungarala Sankaraiiah.
 Valiagath Mohamed Husain.
 Thayamballi Payyanadan Balakrishnan.
 Akolla Sitaramamurti. Dated 5th October, 1942.
 Mukund Madharnao Deshpande. Dated 6th October, 1942.
 Edalji Dhanjisha Anklesaria. Dated 8th October, 1942.
 Mukund Balvantrai Thakore. Dated 18th October, 1942.

(WITHIN INDIAN LIMITS)

To be Lieutenants

2nd October, 1942

Pramod Kumar Pal.
 Indra Mohan Banerjee.
 Pannakal Othuppu Kuriappen.
 Kiran Chandra Ghosh.
 Pragjee Ramjee Solanki.

3rd October, 1942

Tonda Dayanand Saraswati.
 Sheik Abdul Rahim.
 Callakurehi Gopalrao Padmanabha Rao.

4th October, 1942

Ramesh Chandra Chakravarti.
 Shaikh Mohammad Qoreishy.

5th October, 1942

Narendra Bhushan Das Gupta.
 Puthucode Salasranamier Anantharaman.
 Chakrapany Ramachandra Iyengar. Dated 8th October, 1942.
 Solan Singh Chhabra. Dated 9th October, 1942.
 Shridhar Kashinath Kelkar. Dated 10th October, 1942.

(DENTAL BRANCH)

To be Lieutenants (on probation)

Mohammad Abdul Ghani Mian. Dated 6th September, 1942.

Amjad Hussain Sunhi. Dated 7th September, 1942.

PROMOTIONS

Captains to be Majors

R. R. Prosser. Dated 5th August, 1942.
 F. C. Leach. Dated 24th October, 1942.
 R. D. Scriven, M.C. Dated 28th October, 1942.

LAND FORCES

(Emergency Commissions)

Lieutenants (on probation) to be Captains (on probation)

T. H. Spencer Smith. Dated 28th April, 1942.

11th May, 1942

F. Hunter.	F. A. H. Hall.
J. A. W. Bingham.	G. B. R. Walkey.
M. J. Barry.	N. N. Jovetry-Tereshchenko.
C. Conway.	
J. W. Magner.	R. C. Hallam.
C. R. K. Carroll.	G. Hannigam.

H. V. Knight. Dated 23rd May, 1942.
 S. E. Vincent. Dated 8th June, 1942.
 H. M. I. Davies. Dated 19th June, 1942.
 B. M. Medley. Dated 7th July, 1942.

10th July, 1942

T. Stephens. A. J. McG. Cathro.

20th July, 1942

W. E. Owens. G. Quayle.
 D. Currie. Dated 29th July, 1942.
 J. D. Phibbs. Dated 30th July, 1942.
 C. G. R. Sell. 4th August, 1942.
 A. D. A. Maconochie. Dated 5th August, 1942.
 W. J. Aitken. Dated 13th August, 1942.
 A. M. Merriweather. Dated 27th August, 1942.
 B. K. Chowdhuri. Dated 5th May, 1942.

A. Sen Gupta. Dated 7th August, 1942.
 K. N. Sen. Dated 4th September, 1942.

4th September, 1942

C. S. Sandhu. I. D. Singh.
 S. A. Rahim. S. K. Sen.
 B. Ramachandran. Dated 8th September, 1942.

PROMOTIONS

M. V. Ramanamurti. Dated 13th May, 1942.
 D. R. Bharucha. Dated 18th May, 1942.
 C. R. Krishnaswami. Dated 9th July, 1942.
 M. S. Rao. Dated 7th August, 1942.
 R. K. Sen. Dated 27th August, 1942.

4th September, 1942

M. M. Singh. A. M. Mobsby.
 L. M. Gupta. Dated 5th September, 1942.
 S. M. Ghosh. Dated 8th September, 1942.
 S. C. Chatterji. Dated 7th October, 1942.

RETIREMENTS

Lieutenant-Colonel S. L. Mitra. Dated 9th June, 1942.

Major G. Kelly on account of ill-health. Dated 29th April, 1942.

Notes

SODIUM CHLORIDE TABLETS

MESSRS. SMITH STANISTREET AND CO., LTD., Calcutta, have presented three million tablets of Sodium Chloride as a gift to the Government of India. Two million tablets have been earmarked for the use of the Army and the balance for the Royal Air Force.

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Original Articles

A STUDY ON LEPTOSPIROSIS IN BOMBAY CITY

By M. N. LAHIRI

(From the Haffkine Institute, Bombay)

AFTER the first proven case of leptospirosis in the city of Bombay was reported by the writer (1941a), six more cases have been detected which could be proved positive either by serological methods or by the isolation of leptospiræ. It may be emphasized that these positive cases do in no way represent the true incidence of the disease in the city, where only a few of the many cases that actually occur come under medical observation or are admitted into hospitals. Furthermore, the disease is sometimes likely to assume a very mild form with the result that some cases pass unrecognized, while a few more are wrongly diagnosed as one of the other types of jaundice.

Clinical picture

A review of the literature shows that the symptoms presented by the disease are extremely variable. It is not proposed to give a detailed account of the signs and symptoms of each individual case but only broad clinical manifestations as noted are given below. Sudden onset with rigors, high temperature, headache, and muscular pains were noteworthy features. As the cases came under observation a few days after the onset of the illness, the exact initial temperature could not be determined. Conjunctival congestion is regarded as a characteristic sign, but it was noticed in one case only. Prostration was an important feature and was present in a variable degree in all the patients; in three, however, it was very well marked. The occurrence of hæmorrhages is usually mentioned as an important symptom and in fact the disease actually derived its old name from that symptom. It was, however, absent in all the patients except one in whom epistaxis occurred.

Although cases of leptospirosis without jaundice were reported by Schüffner (1934), Fletcher (1927), and Taylor and Goyle (1931), all the cases in this series had marked jaundice which appeared between the 2nd and the 5th day of the illness. It is not unlikely that future studies will reveal here the existence of the non-icteric type of case. Regarding urinary symptoms, all gradations might be observed from slight febrile albuminuria to complete anuria in severe cases. In the cases under investigation oliguria was met in four of the patients. The samples of urine were very high coloured; this was due to the presence of bile. Further, in four of the patients, repeated examinations of the centrifuged deposit of the urine showed the presence of casts (granular and epithelial) in

remarkable numbers, besides leucocytes and red blood corpuscles. The elimination of the casts continued even for some time during convalescence. None of the cases proved fatal and all of them were of moderate severity except one in which the symptoms were so mild that without laboratory examination the diagnosis on clinical grounds alone would have been difficult.

LABORATORY FINDINGS

Case 1

The patient was seen on the 7th day of illness.

Culture.—Two tubes of Vervoot's medium were inoculated with 0.1 and 0.2 c.cm. of the blood respectively. There was no evidence of any growth and the tubes remained sterile for a period of over four weeks when they were discarded.

Animal inoculation.—A young guinea-pig weighing about 160 grammes was injected intraperitoneally with 2 c.cm. of the blood. The repeated examinations of the peritoneal fluid failed to reveal any leptospiræ. The animal remained alive and well.

Agglutination test.—The serum from a part of the blood used for culture showed a titre of 1:160 against the strain (classical) recovered from the first case previously reported. Two further samples of blood showed a very marked rise of titre. The last one collected on the 18th day of illness reacted to a titre of 1:1,000,000 not only against the classical strain but also against its own strain isolated from urine.

Urine.—Six samples of urine from the 13th to the 18th day of illness were collected. The centrifuged deposits did not show leptospiræ either by dark-ground illumination or in stained films. All the samples were systematically inoculated into guinea-pigs. The one inoculated with the urine of the 16th day of illness showed typical signs and died on the 10th day after inoculation. The culture of the heart's blood of the animal gave a pure growth of leptospiræ.

Protective experiments.—Two guinea-pigs of the same weight approximately were taken. One was injected intraperitoneally with 0.25 c.cm. of the serum from the last sample of blood and the other received the same amount of normal human serum to serve as a control. Half an hour later both were inoculated with 2 c.cm. of a virulent culture of leptospiræ. The one which received patient's serum survived whereas the other succumbed to the infection. The protective power of the serum was similarly tested against the patients own strain with identical results.

Case 2

First seen on the 12th day of illness in a toxic state.

Agglutination test.—The serum from the specimen of blood collected on the day of examination agglutinated to a titre of 1:160 but it was evident from the nature of clumps that the titre would go higher. Three more samples of blood were collected on the 17th, 24th and 35th day of illness, and the titre obtained were 1:10,000, 1:100,000 and 1:300,000 respectively against the strains isolated from the case 1.

Protective experiments.—The serum of the last sample of blood in amounts of 0.25 c.cm. afforded protection to guinea-pigs inoculated with the culture from case 1 as well as a local rat strain of leptospira (classical).

Urine.—Only one sample was obtained. No leptospira was seen in the centrifuged deposit by dark-ground illumination. (Further samples could not be collected as the patient was removed from the hospital.)

Case 3

First seen on the 9th day of illness; did not appear to be very ill.

Agglutination test.—The serum from the blood on the day the patient was seen showed a titre of 1:160 against a classical strain. On the 12th day of illness the titre rose to 1:320 definitely and gave a doubtful

reaction in a dilution of 1:400. (Further examination of blood could not be continued as the patient refused to stay in the hospital.)

Case 4

He came under observation on the 7th day of illness. **Blood culture.**—Two tubes of Vervoot's medium were inoculated with 0.2 and 0.3 c.cm. of the blood respectively. There were no signs of any growth and the tubes remained sterile.

Animal inoculation.—Two young guinea-pigs were each inoculated with 2 c.cm. of the blood. *Leptospira* could not be demonstrated in their peritoneal fluid and the animals remained well for six weeks when they were released.

Agglutination reaction.—The serum from the blood collected on the 12th day of the illness showed a titre of 1:10,000 against the strain from case 1. Two more samples were examined which gave a titre of 1:100,000 and 300,000 respectively.

Urine.—11 specimens were examined from the 9th to the 28th day of illness. The centrifuged deposits of each sample were examined by dark-ground illumination and the sample of the 16th day only showed few degenerated forms of *leptospira*. Five c.cm. from each sample were systematically inoculated into guinea-pigs intraperitoneally and the animal which received the urine of the 19th day of illness developed the infection. A pure growth of *leptospira* was obtained by culturing the heart's blood of the animal almost immediately after death.

Protective experiments.—Two guinea-pigs were inoculated with 0.2 c.cm. of the serum from the last sample of blood and a control pair of guinea-pigs approximately of the similar weight were injected with the same quantity of normal human serum. The pair inoculated with the patient's serum were injected subsequently with 2 c.cm. of the virulent culture isolated from case 1 and case 4 respectively and the control pair similarly received the same amount of the cultures. The pair inoculated with patient's serum previous to the test dose survived, whereas the control pair succumbed to the infection.

Case 5

First seen on the 10th day of illness.

Agglutination reaction.—The patient's serum collected on the same day gave a titre of 1:1,000; subsequently the sample of the 15th day of illness reacted to a titre of 1:100,000 against the classical strain as well as the strain isolated from case 4.

Urine.—Three samples of urine were obtained from the 13th to the 15th day of illness. Systematic inoculation into guinea-pig failed to show any evidence of infection in any of the animals. No *leptospira* were also seen in the centrifuged deposits of the samples either by dark-ground illumination or in stained films.

Protective experiment.—0.25 c.cm. of the patient's serum from the second sample of blood protected guinea-pigs inoculated subsequently with the classical strain as well as the strains isolated from case 1 and case 4. Similarly, the controls with normal serum all died of the infection.

Case 6

First seen on the 13th day of illness.

Agglutination reaction.—The serum of the blood collected on the same day of examination gave a titre of 1:10,000 against the classical strain. Another sample was collected on the 17th day as the patient was leaving the hospital and it showed a titre of 1:100,000 against the strains isolated from case 1 and case 4.

Urine.—Two samples of urine were obtained on the 15th and 17th day of illness. No *leptospira* could be detected in the centrifuged deposits by dark-ground illumination but both the samples produced infection in the guinea-pigs. The organism was isolated by culture of the heart's blood of the animals.

Protective experiments.—The second sample of the patient's serum in quantity of 0.2 c.cm. protected

guinea-pigs inoculated subsequently with the culture isolated from case 1, case 4 as well as its own strain. The experiment was repeated twice and similar results were obtained. The control animals inoculated with normal serum and cultures all succumbed to the infection.

Discussion

The isolation of the organism is undoubtedly the most certain method for the diagnosis of the disease. Blood culture is likely to prove positive when carried out within the first week of illness. This method, in the hands of Taylor and Goyle (*loc. cit.*) in the Andamans, yielded a large number of positive results. In the present investigation the method was, however, found to have limited application since the majority of the cases came under observation at a time when the infective period of the blood had already passed. In two of the cases blood was cultured on the 7th day of illness, with negative results. This observation corroborates that of Davidson and Smith (1939) who stated that in their experience the recovery of the organism by blood culture on the 7th day of illness was possible in exceptional cases only. Further, it could not be assured that the date of the onset of illness as stated by patients was accurate.

After the first week of infection, *leptospira* are excreted in the urine, and it is sometimes possible to demonstrate the presence of the organism in the centrifuged deposits. Their morphology, however, is so atypical that no reliance can be placed on such findings. In the author's experience, out of the many samples of urine examined, degenerated *leptospira* were seen by dark-ground illumination in one specimen only; but animal inoculation with such urine samples proved of definite value for the isolation of the organism during the present investigation. In this connection it may be mentioned that the *leptospira* are excreted intermittently, and even samples containing the organism may not prove infective to animals, because the usual acid reaction of the urine as well as the presence of bile in it considerably devitalize the *leptospira* present. For these reasons urine inoculation in animals should be persistently carried out for the successful isolation, although the method involves the use of a large number of animals. For instance, in case 4, out of eleven samples only one produced the infection. On the other hand, in case 6, two samples were obtained and both proved infective.

Of the serological tests, the agglutination reaction was found to be of great aid in diagnosis. It is a method of more practical value in view of the fact that while the blood culture method requires at least a week for the organism to grow, the diagnosis can be made the same day by agglutination tests when the blood is collected after the 7th day of illness. A titre of 1:100 is definitely suggestive of infection. Recently, Packchianian (1941) with the help of the agglutination test detected forty

new cases in U.S.A. Sera from many patients in whom the disease could be excluded failed to react even in a low dilution such as 1 : 20 against the classical strain of *L. icterohæmorrhagica*. The test should, however, be repeated not only to demonstrate the rise of titre but also the end titre. This was considered desirable since Das Gupta (1938) reported agglutination reaction in two of his cases at Calcutta where quite different results were obtained during the earlier phase of the disease and during late convalescence. On a single test, an erroneous conclusion would have been arrived at in regard to the serological type of the leptospira responsible for the infection. By the repetition of the test the para-specific agglutination, if any, could be avoided when strains of various serological types are used. In the present cases the final titre rose very high, i.e., beyond 1 : 100,000.

About the end of the second week of illness and also during convalescence, spirochætocidal antibodies appear in the blood. Such sera have been found to exert a protective action on guinea-pigs. Where isolation of the organism becomes difficult, the test is also helpful in establishing the diagnosis. All the sera used in performing the test were of high agglutination titre, i.e., over 1 : 30,000. Although the agglutination titre does not truly express the value of the protective antibodies, the experiments of Zimmermann and Arjona (1934) suggest that the two more or less go together. A point worthy of mention is that the cultures used for test inoculations should be virulent enough to kill the guinea-pig within six days.

As regards susceptibility to infection it is suggested that very young animals should be used. In the course of the study, certain guinea-pigs here were found to be refractory to infection. On two occasions it was further observed that the inoculated guinea-pigs survived, although leptospiræ could be demonstrated in their peritoneal fluid. Similar observations were reported by Das Gupta (*loc. cit.*) and this shows the importance of the repeated examinations of the peritoneal fluid.

Epidemiological observations

The cases occurred sporadically in different localities of the city. All the affected persons were adult males between twenty and forty years of age. The incidence so far does not show any relation with any particular occupation as was observed by Buchanan (1927) among the miners in Scotland and by Davidson and Smith (*loc. cit.*) among the fish-workers in Aberdeen. There is also no evidence to indicate that the infection could have been acquired by contact with polluted water. The premises of the patient were carefully inspected and they were found to be heavily rat infested. Also, the surroundings were very insanitary. Since these patients usually walk bare-footed for most of the day, it is quite probable that the infection had taken place through abrasions on the skin coming

in contact with rat's urine. It is also quite possible that the infection might have been acquired through the ingestion of the organism with food. Although the feeding experiments of Buchanan (*loc. cit.*) carried out on the guinea-pig do not lend support to this idea such a possibility cannot be ignored. A survey of the rat population of the city (Lahiri, 1941) has shown that of the rats examined, 12 per cent were found to be infected. In addition, the pathogenic strains isolated from rats were found to be serologically identical with the strains isolated from patients. These observations, therefore, strongly suggest that the rat plays an important part in the transmission of the disease. As during the period of about six months, seven genuine cases were detected, it appears likely that the disease is more common in this city than was supposed.

Acknowledgments

I thank the staff of the Gocul Das Tejpal Hospital, the Nair Hospital and the City Fever Hospitals, Arthur Road, for giving me every facility to carry out this investigation. I must also thank Dr. Thosar, Medical Officer-in-charge of the Municipal Dispensary, Souter Street, for inviting my attention to one case. I wish to express my indebtedness to Dr. B. M. Das Gupta, Professor of Protozoology, School of Tropical Medicine, Calcutta, for confirming my results.

Summary

1. Six cases of leptospirosis were recognized during a period of six months. The diagnosis in each case has been confirmed bacteriologically.
2. The *L. icterohæmorrhagica* of the 'classical' group is the serological type of leptospira so far responsible for the infection.
3. The disease occurs sporadically in the city and that the infection is acquired through the agency of rat is discussed.

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REPORTING A NEW FORM OF RAT-BITE FEVER OR SODOKU IN BOMBAY (THE GUMMATOID FORM)

By R. J. VAKIL, M.D., M.R.C.P., D.T.M. & H.,
F.R.F.P.S.G., J.P.

(From the K. E. M. Hospital, Bombay)

THOUGH referred to in the ancient writings of Japan, rat-bite fever was described in detail for the first time by Katsura in 1892. It was not until 1902 that a description of the disease was published in a European language by Miyake who referred to the disease as Rattenbisskrankheit. Within the last forty years, a voluminous literature has appeared on the subject, especially in France.

Vakil and Shah (1942) drew attention to the presence of several tender, 'gummatous' or 'gummatoid' lumps within the muscles and periosteum during the febrile stage of the disease. After indicating the extreme rarity of such a manifestation, they suggested that the case in question might be representative of a hitherto undescribed form of rat-bite fever. Since that time, a further case of this type, with a large, tender lump in the muscle of the left thigh, has been reported (Patel, 1942). In view of the extreme rarity of this type of rat-bite fever, I have thought it worth while to present the clinical reports on two more cases of this type:—

Case 1.—A Hindu male, aged 45, was admitted to the King Edward Memorial Hospital on 25th September, 1942, with a three days' history of fever and 'lumps'. He had been bitten by a rat eight weeks before admission. About seven weeks after the bite, he observed a rise of temperature and the development of the following 'lumps' or swellings: (a) two distinct, localized, firm, tender and painful swellings in the calf-muscles of the left leg; (b) a red, tender and localized induration of the right forearm, without the actual development of nodules; there was a superficial resemblance to a cellulitis.

On admission, his temperature was 102°F., pulse rate 118 and respirations 28 per minute. The urine was normal. A blood count showed 9,700 white blood cells, with 73 per cent polymorphonuclears, 25 per cent lymphocytes, 2 per cent mononuclears, and no eosinophils.

The patient was put on septanilam tablets (Glaxo), two tablets three times a day. The temperature touched normal for a few hours but went up again to 102.8°F.; there was no improvement in the clinical condition, nor any reduction in the size of the 'lumps', but a new lump, tender and painful, had made its appearance in the muscles of the left forearm.

After one injection of novarsenobillon (0.15 g.) on the 29th, the temperature came down to normal and the lumps showed a definite diminution in size. After the second injection of novarsenobillon (0.6 g.) on the 6th October, the lumps disappeared completely within a day or two. The patient was discharged from hospital free of all symptoms and signs.

Case 2.—A Hindu male, aged 41, was admitted to the hospital on 9th August, 1937, with a history of irregular fever, extreme lassitude and frequency of stools (about 10 to 12 stools a day). He had been bitten by a rat on the right forearm. About fifteen days after the bite, he had developed a rise of temperature and a large 'lump' at the site of the bite. This was followed in a day or two by another large lump within the musculature of the left leg. The lump in the left leg was tender to touch, fairly firm to the feel and about 4 inches in diameter.

He was given an intramuscular injection of sulfarsenol (6 cttg.) on the 13th. The temperature, which was about 101.5°F., touched normal on the same day. The injection was repeated on the 14th; by the 16th, the muscle lumps had disappeared completely and the man was discharged fit and well on the 18th of August.

In order to make this case study complete I append a short summary of the two previously reported cases of this type:—

Case 3.—(Vakil and Shah, *loc. cit.*): A Muslim male, aged 40, was admitted to the K. E. M. Hospital on 13th December, 1941, for fever and pains in the muscles and joints of the body. Soon after being bitten by a rat (on the left leg), he had developed high fever, mental depression, œdema of the left leg and pains all over the body. After two injections of sulfarsenol, he was back at work apparently cured. After an interval of three weeks, he had a return of high fever, lassitude and severe pains. On examination, he showed (1) a spherical, smooth, hard and tender lump, about 3 inches in diameter, within the muscles of the left thigh; (2) a tender lump, 1½ inches in diameter, in the left pectoralis major muscle; (3) a small lump, 1 inch in diameter, within the musculature of the right arm. The blood Kalin was 'two-plus'. The total white blood cell count was 10,000 with 72 per cent polymorphonuclears, 20 per cent lymphocytes and 8 per cent mononuclears. He was cured completely within a period of two days by two intramuscular injections of sulfarsenol.

A further follow-up of this case has revealed the surprising fact that the patient has had, after discharge from hospital on the 29th December, 1941, as many as nine distinct attacks of 'fever' with æsthenia and muscle-pains, at intervals of exactly three weeks. Since the rat bite in December 1941, he has had, at intervals of three weeks, eleven attacks of fever (each lasting about three or four days and attaining a peak of about 103°F.). During the 7th attack of fever, he developed tender and painful 'lumps', about 2 or 3 inches in diameter, within the muscles of the left leg and left arm. He also had a large swelling, about 4 inches in diameter and tender to the touch, apparently arising from the periosteum over the anterior aspect of the left femur.

The 9th attack of fever was accompanied by an enormous enlargement of the sub-mental glands.

Case 4.—(Patel, *loc. cit.*): A Hindu male, aged 50, developed high temperature, severe mental depression and muscle- and joint-pains about two weeks after a rat bite on the left foot. Two weeks later, he developed acute bronchitis and low fever, for which he was admitted to hospital. The white cell count was 18,000 with 85 per cent polymorphonuclears, 12 per cent lymphocytes, 2 per cent mononuclears and 1 per cent eosinophils.

The temperature came down to normal after four days of sulphapyridine treatment. In view of the leucocytosis and severe muscle-pains, he was given two intravenous injections of novarsenobillon (on 23rd September and 2nd October). In spite of these, he developed, during the night of the 14th October, a large, firm, tender and freely movable swelling in the middle of the left thigh; the skin over the swelling being warm, a suspicion of abscess was aroused. The temperature was now 99.6°F. while the total white cell count was 20,000 with 85 per cent polymorphonuclears. After two intravenous injections of novarsenobillon (0.3 g. each), the lump in the thigh had disappeared, except for a slight induration of the muscle fibres on deep palpation.

A review of the reported cases

In view of the definite history of rat bite in all the cases, the dramatic response to arsenical derivatives (such as sulfarsenol and novarsenobillon) and the characteristic type of febrile

attack with lassitude, asthenia and muscle-pains, we have no hesitation in regarding these cases as cases of rat-bite fever. The following features, in these cases, are sufficiently characteristic or unusual to warrant comment: (1) The most striking feature of all, and the one that is shared by all the cases is the presence or development of 'gummatoid' or 'gummatous' lumps within the muscles of the body. These 'lumps' or swellings are characteristically tender to the touch and firm to the feel; have a smooth surface, are about 1 to 4 inches in diameter, and, as a rule, are freely movable and unattached to the deeper structures. The lumps, which may cause the patient considerable discomfort or pain, are, as a rule, widely disseminated and bear no relation to the actual site of the rat bite. They may vary in number from one to six; in case 4, there was only one lump, in the middle of the left thigh, while case 3, during the 7th paroxysm of fever, showed as many as six lumps at one time. (2) Case 3 showed, during the 7th attack of fever, a large and tender swelling arising from the anterior surface of the left femur, presumably from the bony periosteum. Periosteal or subperiosteal lumps were not observed in any of the other cases. (3) Swellings of inflammatory type were observed in cases 1 and 4; in case 1, there was a red and tender induration of the right forearm, which appeared, at first sight, to be of inflammatory nature (? cellulitis); in case 4, the swelling in the middle of the left thigh was warm enough and tender to arouse the suspicion of an abscess. (4) In all the cases in which a blood count was carried out, there was observed a mild or moderate degree of leucocytosis (9,700 white cells in case 1, 10,000 in case 3 and 18,000 to 20,000 in case 4). (5) The persistent nature of the infection in case 3 is exceptional. The usual course of events in cases of rat-bite fever is for the infection to die out completely and permanently after a few injections of arsenicals. In this unusual case, there have until now been as many as ten distinct relapses after the initial attack of rat-bite fever, in spite of adequate specific therapy. (6) The conspicuous enlargement of the submental lymph glands in case 3 deserves mention.

Discussion

After a study of these four case reports, one is left in no doubt about the existence of a distinct type of rat-bite fever characterized by the development of peculiar 'gummatoid' or 'gummatous' lumps or swellings within the muscles and in relation to the periosteal linings of the body. This type of rat-bite fever has not been mentioned in any of the textbooks of medicine, nor is there any mention of such cases in the wide literature on the subject of *sodoku*. As far as I have been able to ascertain, these cases of rat-bite fever (with gummatoid swellings within the muscles of the body) are the only ones of their kind reported.

There are frequent references in the literature on *sodoku* to cutaneous manifestations, such as urticaria and macular eruptions. In '*Maladies Infectieuses et Parasitaires*' (1924) there is a description given of certain painful and subcutaneous lesions which may arise in cases of rat-bite fever: 'des papules de la dimension d'une lentille ou d'une pièce de 2 francs, enfin par un semis de nodules sous-cutanés très douloureux, gros comme des amandes.'

Grenet and Lehucher (1918), whilst referring to 'muscle-tenderness' in this disease, have made a passing reference to the occasional association of 'induration' with such tenderness. In 1925, a case of rat-bite fever was reported by Ebert and Hesse of Berlin, associated with spondylitis and perichondritis of the rib-cartilages.

While describing the manifestations of inoculated *sodoku* in rats, McDermott (1928) describes the disease as presenting the following successive phases: (1) an incubation period, (2) a 'primary' inflammatory lesion, with the organisms confined to the lesion itself and to the regional lymph glands, (3) a 'secondary' stage, with organisms in the blood, (4) a 'latent' stage, with no organisms, (5) a 'tertiary' stage, with 'gummatoid' lesions in the lungs, liver, spleen and mediastinal lymph glands. There is, however, no reference in this paper to the possible occurrence of these nodules within muscle-tissue or in connection with periosteum.

Summary

(1) A unique association of multiple 'gummatoid' lesions (within the muscles and periosteum of the body) with rat-bite fever is reported for the first time in medical literature, in four cases recently observed in Bombay.

(2) Case 3, reported here, is notable for the remarkably persistent nature of the infection which, in spite of adequate arsenical therapy, has caused as many as ten distinct relapses after the initial attack of fever.

I am indebted to the editorial board of the *Indian Physician* for permission to include in this paper a short summary of case 3 and to Dr. N. D. Patel for the clinical report on case 4.

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Note.—Had the causal organism been isolated from these cases, the unusual findings would have assumed greater importance.—EDITOR, *I. M. G.*

PSEUDO-TUBERCULOSIS OF THE LUNGS WITH EOSINOPHILIA: CONTRIBUTION TO TREATMENT

By RUDOLF TREU, M.D., L.R.C.P.

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IN October 1940 Frimodt-Möller and Barton reported in this Journal on a large number of patients who had been admitted for sanatorium treatment under the mistaken diagnosis of tuberculosis and who were suffering from infiltrative processes in the lungs accompanied by fever, cough and expectoration which was free of tubercle bacilli. The number of these cases was very large and the authors described the condition as essentially benign but chronic, since a check-up of some patients several years afterwards still showed no change of the x-ray and blood-picture.

As to the ætiology of the condition, the authors have not been able to come to any definite conclusion. They believe the origin to be possibly allergic, but admit that quite conceivably many more causes may have to be considered. Syphilis or protozoal infections could be excluded as ætiological factors.

From the extensive survey of Frimodt-Möller and Barton, it is quite apparent that the condition of 'eosinophile lung' is regarded by them as a chronic one not amenable to any specific treatment. In their paper they do not mention any therapeutic measures beyond the routine sanatorium treatment.

Apparently 'eosinophile lung' is a much more common condition in the South of India than in Bengal. During the past years I have very rarely had occasion to observe lung manifestations as described by Frimodt-Möller and Barton and then only from a radiological point of view without a chance of following them up. I therefore think it may be of interest to report on two cases which were long enough under my observation to make it certain that the condition cleared up in a comparatively short time under treatment. The first case I consider to be of special interest as he appears to be the first European affected by this disease and described in the literature.

Case 1.—The patient, a male European, aged 41 years (the age is of some interest too; the disease commonly appears to affect much younger age groups), consulted me for the first time on 24th June, 1941. For 6 to 8 weeks he had been suffering from cough, which was particularly troublesome at night, his temperature was above normal and had been quite often 101 and even higher; he felt quite weak and unable to continue his work; and he had lost at least 1½ stone in weight. He suggested himself that he might be suffering from tuberculosis as all his symptoms seemed to point to this diagnosis.

Clinical examination of the lungs showed no zones of dullness on percussion, and on auscultation the breathing appeared over both lungs slightly broncho-vesicular with lengthened expiration with many musical rhonchi over both lungs, somewhat reminiscent of asthma bronchitis.

A skiagram taken on the same day showed very extensive mottling over both lungs, fairly evenly dis-

tributed, and intense striation, also without any pre-selection. In fact, the picture somewhat resembled one of extensive silicosis except for the shadows being less dense than in a silicotic lung. But obviously the picture differed vastly from that of a tuberculous infection (figure 1).

The sedimentation time (Linzenmeier) was 24 minutes.

Blood count: hæmoglobin 90 per cent, red cells 4.78×10^6 , WBC—23,400, differential count: neutrophils 21 per cent, lymphocytes 40 per cent, monocytes 3 per cent, eosinophils 62 per cent. Repeated examinations of the sputum showed no acid-fast bacilli, Wassermann and Kahn tests were negative. In the stool motile *Giardia lamblia* were found, but otherwise the stool showed no evidence of inflammatory changes of the colon.

The patient was advised to take rest and treatment was instituted with 30 grains of potassium iodide daily and injections of 'pulmochin'. Up to the 8th of July nine such injections were given, but there was no noticeable effect. The temperature was as high as before, cough and expectoration remained unchanged.

On 8th July the patient was also seen by Dr. A. C. Ukil who confirmed the diagnosis and who also confirmed that he had not yet seen this disease in a European. The treatment with potassium iodide having been without result, it was decided to try arsenic and I chose acetylarsan. The patient received 1 c.cm. on 10th July, 2 c.cm. on 12th July, 3 c.cm. on 14th July, and from then onwards every third or fourth day 3 c.cm. intramuscularly, altogether 13 times. On 17th July another skiagram was taken which did not differ materially from the first skiagram (figures 2 and 2a), but the eosinophilia had fallen to 53 per cent. From the 17th of July the fever stopped and the patient felt better from day to day. The cough and expectoration disappeared and within three weeks he put on four pounds in weight while during the preceding three weeks he had lost a further three pounds in spite of complete rest. From the end of July examination of the lungs no longer showed anything abnormal, the sedimentation test on the 6th of August showed the remarkable improvement from 24 minutes to two hours.

Blood examination on 25th August, 1941, showed leucocytes 6,250, and only 8% eosinophil cells, and the skiagram on 27th August showed that the condition had cleared up to such an extent that the skiagram could only be described as normal (figure 3).

At the beginning of September the patient went for a long leave to South Africa where he consulted several tuberculosis specialists who found his lungs perfectly normal. He was apparently the first case of this type they had come across, this affection being unknown in South Africa. On examination after his return to India on 10th June, 1942, he had regained his old weight, felt and still feels perfectly fit, a skiagram of his lungs shows no pathological changes whatsoever, and his eosinophil cells were 4 per cent.

Case 2.—This patient, a 45-year-old Goanese, consulted me first on 18th October, 1941, with a history of an old tuberculosis of the lungs in 1926. Now he had been ill again for two months, coughing heavily, there was a great deal of expectoration and his temperature rose daily to 100 and even 102°F. He had lost about one stone in weight and felt unable to carry on his duties as clerk. On clinical examination, there was some dullness over his right apex, the breathing sounds over both lungs were broncho-vesicular, and scattered over both lungs were numerous musical rhonchi. The clinical picture was that of a subacute febrile bronchitis, but not of active tuberculosis. There were no tubercle bacilli in his sputum, his sedimentation time was 80 minutes (Linzenmeier). Radiologically he showed evidence of an old fibrotic tuberculosis of the right apex and the upper parts of the right lung and a well-marked increase of the broncho-vascular markings as would be expected in such a condition (figure 4). He did not show radiologically the changes of case 1. Treatment directed against this subacute bronchitis with inhalations, calcium injections, application of liniment, etc.,



Fig. 1.

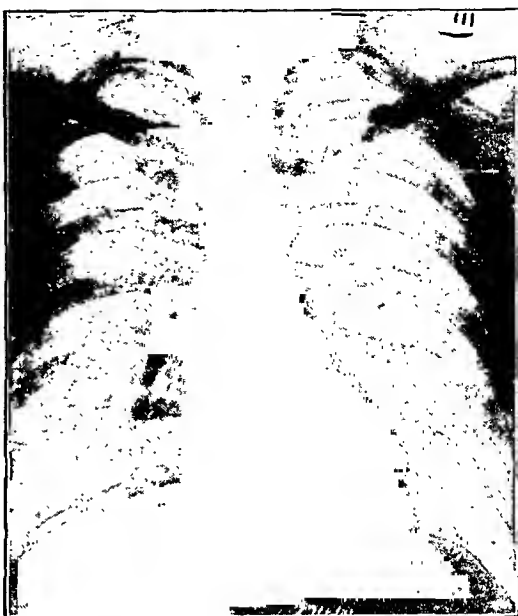


Fig. 3.

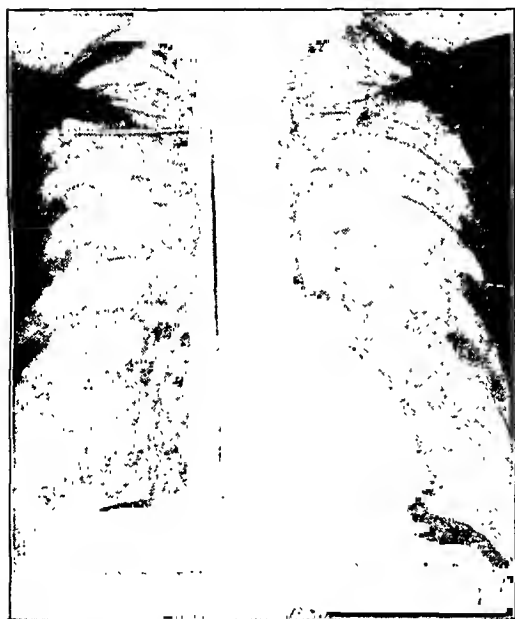


Fig. 2.



Fig. 4.



Fig. 2a.



Fig. 5.

PLATE VI

RUPTURE OF THE LEFT VENTRICLE: REPORT OF TWO CASES:
BALKRISHNA RAO & NATARAJAN. (M. H. P., PAGE 96.)



Fig. 1.—Heart with pericardium showing the diverticulum (a), and a probe in the rupture (b).



Fig. 2.—Heart showing two ruptures (a, b).

A CASE OF BRONCHOGENIC CARCINOMA: R. SUBRAMANIAM. (M. H. P., PAGE 91.)

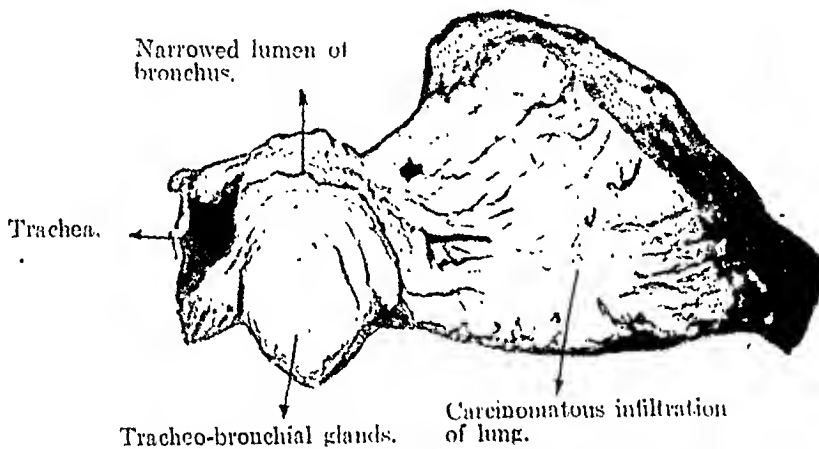


Fig. 1.—Specimen of a slice of the lower lobe of the right lung with a portion of the trachea at the level of the bifurcation.

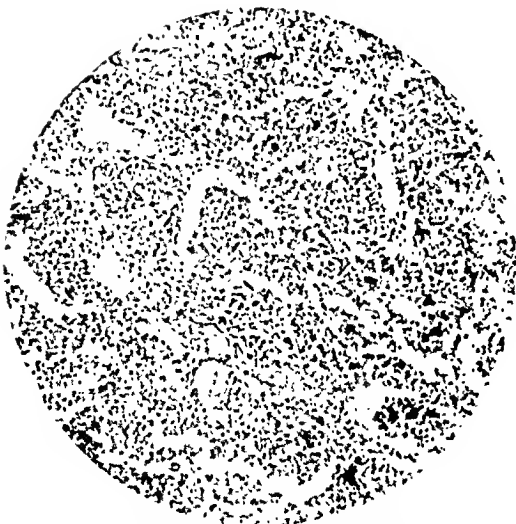


Fig. 2.—Low power photomicrograph of carcinoma of lung.

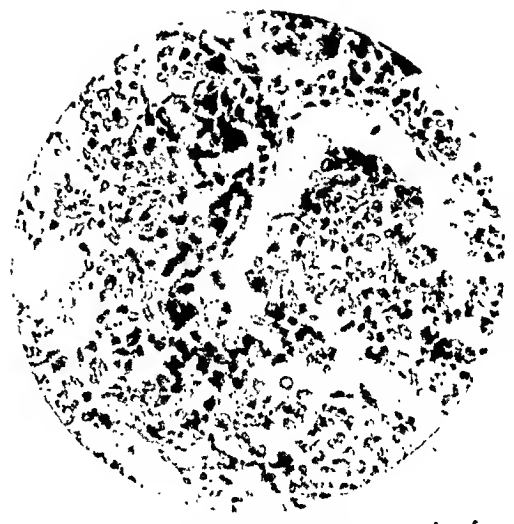


Fig. 3.—High power photomicrograph of carcinoma of lung.

remained entirely unsuccessful, and therefore on 8th November, I considered the possibility that his condition might be better explained by an eosinophile . . . His total leucocyte count was . . . count was 19 per cent neutrophils, 8 per cent lymphocytes, 72 per cent eosinophiles, 1 per cent monocyte. On the same day treatment was begun with 2 c.cm. acetylarsan, followed by 3 c.cm. on 14th and 17th November.

On the evening of the 18th November the patient whose temperature had been normal during the last three days developed high fever. His temperature went up to 105°, and on the next day there were signs of a lobar-pneumonia of the left lower lobe. He was treated with sulphapyridine and was free of fever from 22nd November. Blood examination on 25th November showed an eosinophilia of only 13 per cent and the temperature never rose again. His cough and expectoration disappeared entirely after this attack of pneumonia. His blood examination on 25th November showed leucocytes 9,400, with 13 per cent eosinophile cells. Skiagram taken on 25th November showed the remnants of the pneumonic process of the left lower lobe (figure 5) and strong adhesions of the medial part of his left diaphragm which had disappeared when again examined radiologically on 25th December.

The patient was seen again on 14th June, 1942, after his return from Goa where he had been on holiday since the end of December 1941. Cough and expectoration had been absent since he left Calcutta, his lungs were clinically free of bronchitis, his blood picture had returned to normal, eosinophile cells were 4 per cent.

These two cases have a number of features in common: the longstanding cough with a great deal of expectoration, fever, loss of weight. But, while in case 1 the radiological appearance of the lungs led at once to the correct diagnosis, it was some time before case 2 was properly recognized. The skiagram in case 2 showing an old tuberculosis together with the history of a tuberculous affection of the lungs many years ago seemed to explain all the symptoms well enough, until the examination of the blood proved the actual nature of the disease. And in case 2, although clinically in no way different from case 1, there was no evidence of any changes of the lung-parenchyma beyond those expected in any case of longstanding bronchitis.*

Unfortunately, an intercurrent pneumonia interfered with the treatment by acetylarsan which had given such convincing results in case 1. But this pneumonia also brought the disease to an end as all symptoms and signs of the disease disappeared from the time the pneumonia healed. It is not difficult to assume that the pneumonia in 'eosinophile lung' acted as a severe protein-shock therapy and, since apparently very little is known about any successful treatment of this condition, this fact might encourage others to try some of the well-recognized methods of unspecific shock-therapy in similar cases.

Although I am well aware that one single case proves very little, the success of acetylarsan in case 1 was so immediate and convincing that I feel that case 1 alone is worthy of record for this reason alone. This one observation, it may

(Concluded at foot of next column)

*It is difficult to see how the diagnosis in this case is justified; 'idiopathic' eosinophilia is very common in this country.—EDITOR, I. M. G.

CATARACT IN UNTREATED CASES OF DIABETES MELLITUS

By M. A. SHAH, M.B., B.S., F.C.M.S.

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ALTHOUGH in 1778 Rollo (Duke-Elder, 1941) mentioned that patients suffering from diabetes were especially prone to get cataract, a systematic description of the condition did not appear till 1834 when Berndt published his description (Kirby, 1933).

Two types of cataract have been defined clearly in our times by Duke-Elder (*loc. cit.*) but it must be pointed out that references to these types are not wanting in the writings of earlier authors, especially in those of Beard in the middle of the last century. The types are:—

1. Senile cataract coming on in diabetes.
2. A true diabetic cataract, which is very rare.

Senile cataract in diabetic patients.—The changes in the lens are mainly the same as those occurring in senile cataract in old people. There are, however, some differences in the incidence, the time of appearance, and the rate of progress of these lenticular opacities.

In order to obtain some idea of cataract occurring in untreated diabetic patients in the Punjab, a series of 36 patients suffering from diabetes mellitus was examined in the eye out-patients department of the Mayo Hospital, Lahore. None of the patients examined had ever had any treatment for their diabetes; this fact was due mainly to ignorance or to economic reasons. The duration of the disease was recorded as far as was known to the patients. The urine was examined for sugar, but the blood sugar during fasting could not be estimated, in view of the limited scope of the present investigation. The cases of diabetes were divided into 5 classes:—

1. Very mild when sugar was present in traces.
2. Mild when it was $\frac{1}{2}$ to 1 per cent.
3. Moderate, 1 to 2 per cent.

(Continued from previous column)

be hoped, will encourage others to try acetylarsan in similar cases and it may open the way to a remarkable shortening of this otherwise essentially chronic disease.

Summary

Two cases of clinically almost identical but radiologically quite different forms of pseudo-tuberculosis of the lungs with eosinophilia are described.

The first case showed the typical radiological appearance of mottling of the lungs, while the second case showed no typical evidence of this disease but showed evidence of old fibrotic tuberculosis.

The first case was successfully treated with acetylarsan, the second case healed after an intercurrent lobar-pneumonia which began after only three acetylarsan injections had been given.

4. Moderately severe, 2 to 5 per cent.
5. Severe beyond 5 per cent.

Each patient was examined in the dark room, the pupils having been dilated with homatropine. The methods employed were oblique illumination, plain mirror at reading distance, indirect and direct ophthalmoscopy. In addition to lenticular opacities, careful examination was made of the vitreous for opacities, the retinal blood vessels for arterio-sclerosis, and the retina for any hæmorrhages.

The investigation under report was carried out on lines similar to those of Kirby (*loc. cit.*) and for comparison his results are also given in the tables.

Sex incidence.—In the present series of 36 patients there were only 9 females and 27 males, i.e., the proportion was 3 males to 1 female. Kirby found females to suffer three times as much as males.

Frequency of cataract in diabetes.—Out of 36 patients 24 (66.6 per cent) were found to be suffering from lenticular opacities. In a series of 50,438 patients attending the eye out-patients department for various eye troubles, 3,284 (6.4 per cent) had cataract. It appears, therefore, that patients suffering from diabetes are 10 times more likely to get cataract than those not suffering from this disease. This is in agreement with the findings of Kirby who reported 64 per cent of the diabetics suffering from lenticular opacities as compared to 5 to 12 per cent of the non-diabetics.

Incidence of cataract in relation to age.—Up to the age of 40, of 9 cases examined 3 (33 per cent) had cataract; between 40 and 45, out of 6 cases 3 (50 per cent); between 60 and 70 out of 18 cases 15 (83.3 per cent); at 70 years of age and above 3 cases were examined but none had cataract. It would appear that the incidence of cataract increases with age and is highest between 60 and 70 years. Kirby's conclusion was that the incidence decreases as age advances.

Relation of cataract to the duration of the disease.—This is variable. Six cases of 2 years' duration were examined and 5 had cataract (83.3 per cent). There cases of 3 and 4 years' standing were examined, and cataract was found in 2 cases in each group (66 per cent). In 3 cases of 5 years' duration only 1 had lenticular opacities (33.3 per cent), while 21 cases of duration more than 5 years were examined, and 12 (59 per cent) had cataract.

The severity of the disease appears to have little influence on cataract formation. Six cases of very mild diabetes showed 1 case of cataract (16.6 per cent), 12 cases of mild diabetes with 10 cases of cataract (83.3 per cent), 15 cases of moderate diabetes showed 1 case of cataract (33 per cent). The frequency of these types of diabetes is shown in tables I and II.

TABLE I
Types of diabetes

Country	Very mild	Mild	Moderate	Moderate severe	Severe
America	15.0%	24.0%	35.0%	17.0%	9.0%
Punjab	15.3%	30.6%	38.4%	6.6%	6.6%

TABLE II
Incidence of cataract in relation to severity of disease

Country	Very mild	Mild	Moderate	Moderate severe	Severe
America	40.0%	66.0%	66.0%	50.0%	50.0%
Punjab	16.6%	83.3%	60.0%	0.0%	33.0%

The forms of lenticular opacities were variable but senile cortical cataract (68.9 per cent) predominated. Six cases out of 36 (20.6 per cent) had nuclear cataract, 2 (6.8 per cent) posterior cortical, and none had subcapsular opacities (table III).

TABLE III
Types of lenticular opacities

Country	Senile cortical	Nuclear	Post-cortical	Subcapsular
America	70.0%	21.0%	7.0%	2.0%
Punjab	69.9%	20.6%	6.8%	0.0%

Some of the patients with diabetes have other complicating diseases such as arteriosclerosis, retinal lesions (Kirby, *loc. cit.*), retrobulbar neuritis, hæmorrhagic glaucoma, and iritis, Utthoff and Arruga (Kirby, *loc. cit.*). In the present series, in 5 cases (13.8 per cent) there were definite signs of arteriosclerosis (confirmed later by blood pressure readings). Vitreous opacities and hæmorrhages in the retina were present in three cases (8.3 per cent).

Summary

A report is presented of an investigation into 36 untreated cases of diabetes mellitus with particular reference to the frequency of cataract, its incidence in relation to age, duration and severity of disease, and the forms that such cataracts assume. It is concluded that cataract is far more common in cases of untreated diabetes of moderate severity than in the general population, but is usually of the senile cortical variety. The incidence of retinal and vascular complicating diseases does not appear to be high in such patients.

(Concluded on opposite page)

A STUDY OF TETANUS AND ITS TREATMENT WITH MAGNESIUM SULPHATE

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M.R.C.P. (Lond. and Edin.), D.T.M. (Cal.)

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TETANUS is a fairly common disease in India in hospital practice, but a rarity in general practice. Numerous papers have been published from time to time in which the relative merits of the different methods of treatment have been discussed. The treatment with large doses of antitetanus serum, as advocated by Cole and others, has been very favourably reported upon, and is, consequently, the treatment of choice in these days. The cost of this treatment however is so high that in India it is quite impossible for most people to bear it. The hospitals too cannot afford to provide such large quantities of this expensive serum for the use of their patients.

During a period of four years (1934-1938) I have had the opportunity of treating a large number of tetanus cases in the tetanus ward of the Patna Medical College Hospital. My experience in the ward soon led me to the conclusion that the search for, and adoption of, a cheaper method of treatment was a matter of imperative necessity, particularly in view of the extreme poverty of the average patient and the paucity of funds available for treatment in most Indian hospitals.

Though the prophylactic treatment has been a great success, the treatment of tetanus, once established, is beset with many difficulties. With the appearance of the earliest signs of tetanus, the tetano-toxin becomes fixed to the nerve cells. The neutralization of this toxin, or its dissociation from the nerve cells and neurones to which it is attached, is generally considered to be practically impossible. But certain French authors claim that the administration of chloroform may cause the nerve cells to release the toxin bound to the lipoids of the nerve cells (phylactic theory of Billard) and may thus make possible the maximum antitoxic effect from each injection of antitetanus serum.

Yodh's experience with chloroform was, however, by no means encouraging, as in many

cases it caused pulmonary oedema and proved fatal.

In view of the peculiar nature of the combination of the toxin with nerve cells, the main line of treatment is to maintain the patient's strength by controlling the spasms by the use of sedatives, bromides, chloral hydrate, etc., in large doses. Since sufficiently large doses of the sedatives could often not be used on account of the general debility or poor constitution of the patients, I was anxious to find a sedative which would produce the necessary relaxation and so control the spasms when used in comparatively moderate doses. On going through the literature I was struck by the possibilities of magnesium sulphate.

In this connection Beckman (1934) writes—'Following the preliminary work of Meltzer and Auer (1906) on monkeys, Blake (1906) used magnesium sulphate in the first case of human tetanus in 1906. Since that time it has won many staunch advocates, both in this country and abroad, but it is passed very lightly in most of the textbooks. I wonder why? Perhaps it is the fear that it may encroach upon the partial victory that the antitoxin has won; otherwise I am at a loss to account for the reticence, for surely no physician who has once seen the remarkable relaxing power of this salt upon an agonized tetanus patient can seriously doubt its value even though it may be not in itself curative. Properly employed, rest and comfort and the taking of food are made possible; complete relaxation is not to be sought'.

The view so strongly expressed by Beckman (*loc. cit.*) in favour of the use of magnesium sulphate led me to try out his suggestions in my wards. The patients were therefore given intramuscular injections of a 25 per cent solution of magnesium sulphate, along with two intramuscular injections of antitoxic serum in small doses at an interval of 48 hours. The antitoxin was of course meant to neutralize the toxin which was being produced and was subsequently being absorbed into the circulation. At the same time an attempt was made to lessen the toxic absorption by opening up the pockets of septic foci and flushing them with dilute solutions of oxidizing agents in order to change the anaerobic condition into an aerobic condition, which retards the growth of tetanus bacilli. It is well known that tetanus bacilli grow best under the complete anaerobic conditions prevailing in deep wounds, and that its growth is aided by pus-producing organisms.

The prognosis depends largely on the control of hyperpyrexia and the severity of the associated pyogenic infections.

Method of treatment

As soon as a tetanus case was admitted to the ward, search was made for wounds, otorrhoea, etc., and 9,000 international units of antitoxin were injected intramuscularly round the wound, if present, and the injection was repeated after 48 hours. Wounds were cleansed

(Continued from previous page)

I wish to thank Professor M. Bashir and Dr. R. A. Sayed for help and guidance, and Dr. M. Haq for kindly referring to me the diabetic patients attending the medical out-patients department of the Mayo Hospital, Lahore.

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with hydrogen peroxide, diluted Condyl's lotion or diluted electrolytic chlorine, whichever was available and dressed with sterile dressing soaked in diluted electrolytic chlorine. As the retention of a foreign body increases the chances of tetanus, the wounds were explored under anaesthesia and foreign bodies when found were removed. A mixture containing chloral hydrate gr. x, potassium bromide gr. x, syrup simplex 5i, water to 5i, was given every four hours by mouth. Where feeding by mouth was not possible, nutrient enemata were given with glucose; sedatives such as chloral hydrate and potassium bromide, or paraldehyde by the drip method were given at regular intervals. Nursing activities were reduced to a minimum as they often induced reflex spasms.

As a routine measure all cases received intramuscular injections of a 25 per cent solution of magnesium sulphate, adults receiving 5 c.cm. intragluteally twice daily and the adolescents and children from 4 c.cm. to 2 c.cm. twice daily. In severe cases of tetanus with frequent spasms or convulsions, morphine gr. 1/4 and atropine gr. 1/100 were also injected once or twice daily, the frequency depending on the severity of the paroxysms, and 50 c.c. of a 25 per cent solution of glucose was administered intravenously after each morphine injection. The intravenous administration of glucose serves to restore the glucose content of the tissues which is known to be reduced by more than 50 per cent in the central nervous system of an experimental animal.

Otorrhoea was treated by cleansing the ear with swabs soaked in hydrogen peroxide, and with mercuriochrome drops.

In puerperal sepsis, vaginal douches were given with dilute Condyl's lotion.

In order to ascertain how far the treatment on the above-mentioned lines was effective, I undertook an analysis of the cases, and the tables are presented in this paper in the hope that they will stimulate a more complete and extensive investigation elsewhere. The conditions under which the treatment was carried out were far from satisfactory, as the wards were often overcrowded and not soundproof, and the walls were not painted dark, nor were the shutters placed obliquely to protect the patients from external stimuli.

Before concluding, one is tempted to quote Cole :—

'To compare the results of two methods of treatment of tetanus, it is most important to take two series of cases in which the incubation periods and periods of onset are as near as possible identical, which are as similar as possible in other respects, and in which, apart from tetanus, patients are physically fit. . . . Tetanus is such a variable disease that unless this method of control is used the results obtained in different series of cases are bound to be conflicting.'

Results

The subjects of this analysis are 155 patients admitted consecutively to the Patna Medical College Hospital, in which a clinical diagnosis of tetanus was made. In this series 56 cases of tetanus neonatorum have not been included as none survived in spite of treatment by various methods. For a comparative study, the results are tabulated as follows :—

- I. Sex in relation to aetiology.
- II. Age.
- III. Age in relation to aetiology.
- IV. Incubation period.
- V. Incubation period in relation to regional distribution of injuries.
- VI. Period between onset and hospitalization.
- VII. Mortality rates.
- VIII. Mortality rates excluding deaths within 24 hours.

TABLE I

Sex in relation to aetiology

Sex	Without evidence of injury	Injury	Child-birth	Otorrhoea	TOTAL
Male	45	37		4	86
Female	23	13	31	2	69
TOTAL	68	50	31	6	155

Out of 155 cases treated, 86 were males and 69 females. Excluding 31 females in this series who had tetanus due to infection during or immediately after childbirth, the incidence in the males would appear to be nearly 2.3 times more than that in the females. Since however many females do not seek admission to the hospital, no definite conclusion can be drawn from these figures, regarding the incidence of tetanus in the two sexes. Females are, perhaps, less exposed to tetanus infection.

Age (see tables II and III and figure 1).—The number of cases of tetanus showed a decline with increasing age and it was remarkably low after 30 years. Kini and Rao's experience at Vizagapatam was practically the same. But in Yodh's series from Bombay, the highest number was in the period 21 to 30 years, the next highest in the period 31 to 40 years. Industrial activity in Bombay may account for this, as the wage-earning period is mostly between 21 to 40 years especially for manual labour. The youngest patient in my series was one year old.

Aetiology (see table III).—In this series 68 patients (43.9 per cent of the total) did not show any evidence of injury and formed the largest group; 30 (44.1 per cent) of them belonged to the age period of 1 to 10 years. The youngest patient in this series was one year old, and was taken away from the hospital

TABLE II
Age

Age in years	AUTHOR				KINI AND RAO (1939)				YODH (1937)			
	Number	Cured	Died	Otherwise	Number	Cured	Died	Otherwise	Number	Cured	Died	Otherwise
1-10 ..	49	25 67.5%	12 32.5%	12	9	5 55.6%	4 44.4%	..	78	42 55.2%	34 44.8%	2
11-20 ..	43	23 60.5%	15 39.5%	5	8	5 62.5%	3 37.5%	..	89	42 49.4%	43 45.7%	4
21-30 ..	32	16 59.2%	11 40.8%	5	9	5 55.6%	4 44.4%	..	120	63 54.3%	53 45.7%	4
31-40 ..	18	8 50.0%	8 50.0%	2	6	1 20.0%	4 80.0%	1	101	45 45.5%	53 44.1%	3
41-50 ..	7	4 66.7%	2 33.3%	1	3	1	2	..	44	15 34.8%	28 65.2%	1
Above 50	6	3 50.0%	3 50.0%	..		33.3%	66.7%	..				
Not known	3	2 66.7%	1 33.3%	..	6	2 40.0%	3 60.0%	1
TOTAL ..	155	79 60.7%	41 39.3%	25	38	19 51.3%	18 48.7%	1	438	209 49.4%	214 50.6%	15

within a few hours of admission. Next to him there were two patients who were two years old and both were cured. In this age-period children

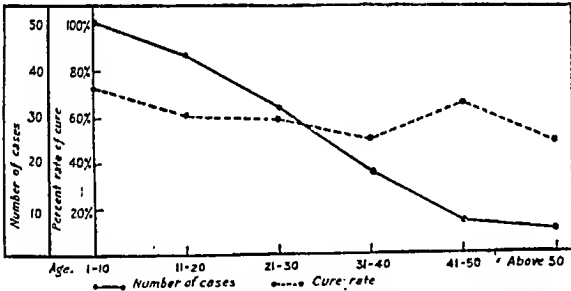


Fig. 1.—Age and cure rate.

often get slight scratches which may get infected and pass unnoticed.

The cases of tetanus with a definite history of injury formed the next largest group, being 50 (32.2 per cent of the total) in number. Of these, 29 (58 per cent) were in the age-group of 1 to 20 years. In this series the youngest patient was 2½ years old.

Childbirth was responsible in 31 (21 per cent of the total) cases. In these cases the incidence was highest during the most productive period of the child-bearing age, namely, from the age of puberty to the age of 30 years. Of the 6 (3.9 per cent of the total) cases, in which otorrhoea was followed by tetanus, 5 (83.3 per cent) belonged to the age period of 1 to 10 years.

Incubation period (see tables IV and V and figure 2).—In a large number of cases the incubation period could not be ascertained as

TABLE III
Age in relation to aetiology

Age in years	NO EVIDENCE OF INJURY				INJURY				CHILDBIRTH				OTORRHOEA			
	Number	Cured	Died	Otherwise	Number	Cured	Died	Otherwise	Number	Cured	Died	Otherwise	Number	Cured	Died	Otherwise
1-10 ..	30	15	7	8	14	8	3	3	5	2	2	..
11-20 ..	14	9	5	0	15	9	3	3	13	4	7	2	1	1	0	1
21-30 ..	14	7	3	4	6	3	2	1	12	6	6	0	0	0
31-40 ..	3	1	1	1	11	6	0	0	4	1	2	1
41-50 ..	4	3	0	1	1	1	0	0	2	0	2	0
51-60 ..	3	2	1	0	2	0	2	0	0
Above 60	1	1	0	0
TOTAL ..	68	37 68.5%	17 31.5%	14	50	28 65.1%	15 34.9%	7	31	11 39.3%	17 60.7%	3	6	3 60.0%	2 40.0%	1

the patients were unable to say when and how the infection might have taken place. Among the cases with known incubation periods, the rate of cure was generally found to be higher in cases where the incubation period was longer.

TABLE IV
Incubation period

Incubation period in days	Cured	Died	Total
1-5 ..	7 43.8%	9 56.2%	16
6-10 ..	10 76.9%	3 23.1%	13
11-20 ..	10 83.3%	2 16.7%	12
Above 20 ..	1 50.0%	1* 50.0%	2

*Died of septicæmia.

Out of 50 cases of injuries with a definitely known incubation period, in 4 (8 per cent) cases the wounds were on the head and neck, in 2 (4 per cent) cases on the trunk, in 14 (28 per cent) cases on the superior extremity, and in 30 (60 per cent) cases on the inferior extremity. The course and prognosis of a case seemed to bear no relationship to the site of injury. The mortality rate varied from 33.3 to 50 per cent.

Period between onset and admission (see table VI and figure 3).—Out of 130 cases, a definite history of onset could be obtained in 97 cases only. As most of the cases came from villages around Patna, the maximum number of admissions was on the third day of the disease.

The longer the period before admission to hospital, the better was the rate of cure.*

*Presumably because the disease was milder.—Ed.

Mortality rates (see tables VII and VIII).—Though I admit that it is fallacious to compare results of one group of cases with another, a comparative study of the mortality rates in consecutive cases, given above, in series of cases treated by different methods by various workers is however of interest. Excluding 25 cases discharged at request, the mortality rate in the series of cases treated by the author, principally with magnesium sulphate and sedatives, was 39.3 per cent, a figure which compares very favourably with those of other workers employing different methods of treatment.

Out of 31 cases (table III) in which tetanus followed childbirth, 11 cases (39.3 per cent) recovered, 17 cases (60.7 per cent) died and 3 cases were discharged at request.

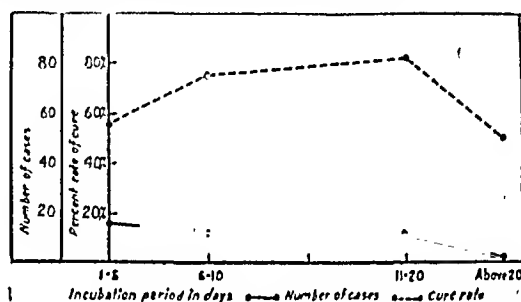


Fig. 2.—Relationship between incubation period and rate of cure.

Cost of treatment

In the method of treatment adopted by the author, the quantity of antiserum needed for each patient was 18,000 units and its cost was approximately Rs. 10 at the present rate of exchange (Re. 1 = 1s. 6d.), whereas in Kini and Rao's series the cost of serum for each patient was much greater.

The cost of the quantity of magnesium sulphate required for each patient for treatment is negligible, and its solution for injection could be

TABLE V
Incubation period in relation to regional distribution of injuries

Incubation period in days.	HEAD AND NECK				TRUNK				SUPERIOR EXTREMITY				INFERIOR EXTREMITY				TOTAL			
	Total	Cured	Died	Otherwise	Total	Cured	Died	Otherwise	Total	Cured	Died	Otherwise	Total	Cured	Died	Otherwise	Total	Cured	Died	Otherwise
1-5 ..	3	2	0	1	2	0	1	1	4	2	0	2	9	4	1	4
6-10 ..	1	0	1	0	..	1	1	0	4	2	1	1	16	8	8	0	23	11	11	1
11-15	7	4	1	2	7	4	1	2	14	9	3	2
16-20	1	1	0	0	1	1	0	0	2	2	0	0
21-30	1	1	0	0	1	1	0	0
Above 30	1	1	0	0	1	1	0	0
TOTAL	4	2	1	1	2	1	1	0	14	8	4	2	30	17	9	4	50	28	15	7
		66.7%	33.3%			50.0%	50.0%			66.7%	33.3%			65.3%	34.7%			65.1%	34.9%	

TABLE VI

Period between onset and admission to hospital, and mortality rates.

Days ..	1	2	3	4	5	6	7	8	9	10	Over 10
Number ..	13	39	15	8	5	2	1	1	1	7	6
Cured ..	6	20	9	7	4	1	1	1	1	6	6
	46.1%	51.2%	60.0%	87.5%	80.0%	50.0%	100.0%	100.0%	85.7%	100.0%	
Died ..	7	19	6	1	1	1*	1†	..
	53.9%	48.8%	40.0%	12.5%	20.0%	50.0%	14.3%	..
Died within 24 hours ..	3	10	2	1	..	1

* Died of pneumonia.

† Died of septicæmia.

easily prepared and sterilized for use in any hospital.

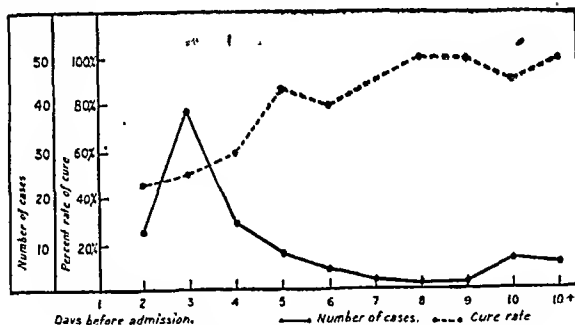


Fig. 3.—Relationship between the day of onset and cure rate.

The average period of stay of a patient in this series was approximately 18 days and the longest period was 32 days.

spasms, and nourishment is maintained, the chances of recovery would naturally improve. Therefore the sooner the treatment is begun, the better for the patient.

There is no difference of opinion about the manner in which the wounds should be dealt with and the foreign bodies removed. But different workers hold widely divergent views regarding the optimum quantity of antiserum which should be used and also regarding the relative merits of the various routes for the introduction of antitoxin. For example, while Cole advocates the administration of a very large dose (200,000 international units) of antitoxin intravenously as soon as possible after the diagnosis has been made, Huntington, Thompson and Gordon (1937) put forward the view that the administration of the antitoxin produces no marked effect at all. Huntington and his co-workers drew their con-

TABLE VII
Mortality rates

	Author	Ghosal and Chaudhury (1942)	Kini and Rao (1939)	Yodh (1937)	Cole (1937)	Huntington and others (1937)	Klopp (1936)
Cases ..	155	35	38	438	30	642	56
Cured ..	60.7% (79)	51.4% (18)	51.3% (19)	49.4% (209)	56.6% (17)	33.9 to 42.4%	28%
Died ..	39.3%* (41)	48.6% (17)	48.7%† (18)	50.6%‡ (214)	43.3% (13)	58.6 to 66.1%	72%

* Excluding 25 discharged at request. † Excluding 1 discharged at request. ‡ Excluding 15 discharged at request.

TABLE VIII

Mortality rates excluding deaths within 24 hours

Author	Ghosal and Chaudhury (1942)	Kini and Rao (1939)	Yodh (1937)	Cole (1937)
	21.7%	25%	18.4%	29.4%
				22.7%

Discussion

In most cases of tetanus, a sublethal dose of the tetanus toxin has already been absorbed into the system by the time the early symptoms of the disease make their appearance. If the further formation of the toxin and its subsequent absorption is stopped by treating the wound and injecting a suitable quantity of the antitoxin, and if exhaustion is prevented by controlling the

exclusion from a study of 624 cases of tetanus which showed a mortality rate of 65.3 per cent in untreated cases as compared to 58.6 to 66.1 per cent in the treated cases.

One cannot, however, deny the utility of the prophylactic administration of antitetanus serum. Beckman (*loc. cit.*) quotes Bazy who reported tetanus in only one case out of a 100 wounded cases in France who had received prophylactic antiserum, whereas 18 cases developed tetanus among the other 100 cases of a similar type who had not received the antiserum. Among the British wounded who had no prophylactic treatment, 53.3 per cent of those who contracted tetanus died of it, whereas in those who did receive the prophylactic treatment but subsequently developed tetanus, the mortality was 22.5 per cent. My experience in the casualty clearing section of the Patna Medical College Hospital has been similar to Bazy's. I

have not seen a person who, having received a prophylactic treatment with antiserum, developed tetanus.

From the above findings it struck me that in treatment it would be better to use slightly larger doses of antitetanus serum than is ordinarily used for prophylactic purposes, namely, three times 3,000 international units, and to repeat it after 48 hours.

The next question is how best to control the spasms? Curare has long been known to control the spasms effectively by paralysing the neuromuscular junctions, but its administration is beset with many difficulties. Florey, Harding and Fildes (1934) controlled the spasms of tetanus in rabbits by injections of curarine (the active alkaloid of curare) at intervals of half an hour. It was also tried in the treatment of tetanus in human beings with inconclusive results. The variation in strength and in the mode of action of different samples of curare makes the problem of its dosage very difficult. A slight overdose or overaction produces respiratory paralysis. A very careful watch over the patient is therefore necessary if the drug is to be used as a routine measure.

In magnesium we have a substitute for curare. The precise way in which magnesium acts is not known. It has been shown that a soluble salt of magnesium, when injected intravenously into a rabbit, produces a complete loss of excitability in all parts of the nervous system; not only is the central nervous system paralysed, but the drug also produces a curariform action and paralyses the motor nerve endings in the voluntary muscles. Magnesium acts upon all parts of the central nervous system alike, unlike most hypnotics which act first upon the higher parts of the brain and produce descending paralysis of the central nervous system. Large doses may cause death by paralysing the respiratory centre. All these effects are, however, immediately abolished by injecting calcium salts intravenously. For its paralysing effects on nerve tissue, the sulphate of magnesium (25 per cent solution) was used in eclampsia, epilepsy, chorea, tetanus, hyperpnea, etc., but it had nearly gone out of use in general practice.

The administration of magnesium sulphate may be effected subcutaneously, intramuscularly, intravenously or intrathecally. Intrathecal injections once daily after anaesthetization with ether were out of the question for me. Intravenous injections are the most dangerous of all, for they may produce sudden respiratory failure. Moreover the effect usually disappears in 30 minutes as magnesium sulphate is excreted rapidly by the kidneys. Subcutaneous injections are very painful. Intramuscular injections are therefore the obvious choice. In my series of cases, intramuscular injections of magnesium sulphate gave complete relaxation lasting from four to six hours. The simultaneous administration of sedatives such as bromide, chloral hydrate and minute doses of morphia

increased the period of relaxation and kept the patients quiet longer.

Wainwright (1926) analysed 760 cases and showed that 80 per cent of them had received their injuries on the street, on the farm, in homes, gardens, stables, etc., and only 20 per cent in industrial accidents.

Tetanus spores are widely spread in nature. The presence of the bacilli and spores, especially in the soil of the cities and inhabited areas and also in the faeces of the farm animals, has been demonstrated by various workers in different countries. It is also a matter of common knowledge that many persons harbour spores in the gut. No doubt from these sources they easily get entry to wounds and abrasions, and grow easily when the wound is a deep one, or is protected by a scab which prevents the permeation of oxygen from the capillaries or the atmosphere. Since conditions favouring its growth are likely to occur from time to time, in small wounds as in large, the disease is met with at long intervals in general practice.

The reason for admission of most of the cases of tetanus on the third day, in my opinion, lies in the fact that the medical aid available to the class of people, who are more commonly infected, is very inadequate. On the first day the early signs are usually thought to be functional, or perhaps a passing phase of some illness. On the second day tetanus may be suspected, but it is not until the third day that tetanus is definitely diagnosed either before removing the patient to the hospital, or in the hospital itself.

Summary

1. A review of 211 cases of tetanus including 56 in new-born babies treated with the combined method of administration of small quantities of antiserum, and magnesium sulphate, with sedatives has been made.

2. The simple mode of treatment followed by the author is described and mortality rates compared with those recorded with other forms of treatment.

3. Observations are encouraging and confirm the suggestion that magnesium sulphate injections will be useful in the treatment of tetanus.

4. Intramuscular injections of a 25 per cent solution of magnesium sulphate controlled the spasms effectively and produced no ill-effects.

5. The administration of bromides, chloral hydrate and also minute quantities of morphia prolonged the period of relaxation.

6. Tetanus neonatorum is a fatal disease.

Acknowledgment

I wish to express my thanks to Rai Bahadur Dr. T. N. Banerjee, professor of medicine, for the encouragement and Rai Bahadur Dr. R. P. Ghosh, superintendent of the Patna Medical College Hospital, for permission to publish this article. My thanks are also due to Professor T. N. Seth and Dr. S. K. Ray for assistance in the preparation of this article, and to my

(Concluded on opposite page)

THE RESULT OF AMPUTATION OF A LIMB FOR FILARIAL LYMPHANGITIS AND ELEPHANTIASIS

By S. SUNDAR RAO

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AMPUTATION of the elephantoid limb is recommended by several workers when the limb has become riddled with abscess cavities and sinuses or where gangrene threatens with consequent danger to patient's life (Connor, 1929; Chatterji, 1927). In such cases, there is ample justification for doing an amputation. More frequently, however, an amputation is carried out to remove a disability due to the heaviness of the elephantoid limb (Chatterji, *loc. cit.*). Nevertheless, there is also a feeling that amputation of the affected limb is a measure of treatment of filariasis. Maitland (1891) says that 'when the health of the patient is harassed by constantly recurring attacks of inflammation, the limb must be amputated'. This seems to indicate that amputation would cure the patient of filariasis.

In India, it is only very rarely that amputation of the limb is resorted to in cases of filariasis. In none of the cases in which amputation was carried out has the subsequent history of the patient been reported. I have recently come across a young and robust man who had a moderate elephantiasis of the leg and who had his leg amputated in 1923. The history of this case is of interest.

(Continued from previous page)

successive house physicians for their co-operation and the case notes.

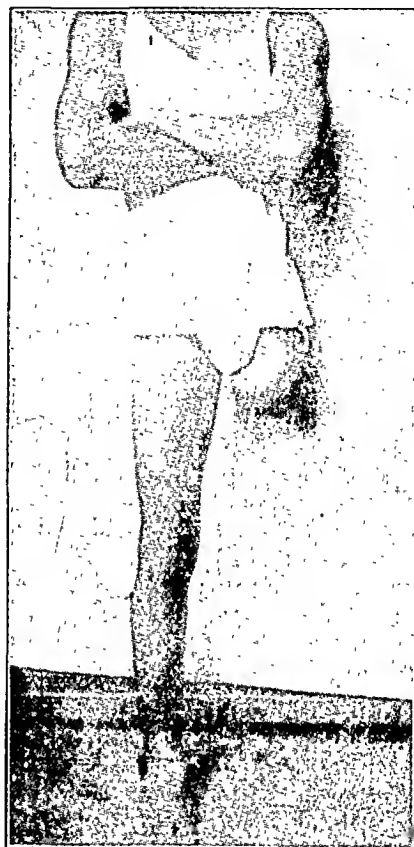
[Note.—The figures quoted in this paper indicate, but the paper does not clearly state, that the severe cases (short incubation, early severity of symptoms and consequently early hospitalization and early treatment) show a high mortality, while the milder cases (longer incubation, later hospitalization and late treatment) show a high recovery rate. Other workers have reported similar findings. Treatment is of value but its value is limited.—EDITOR, I. M. G.]

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Case report

K. G., male, aged 34, Hindu, tailoring business, Calcutta. The first attack of filarial lymphangitis appeared in the left leg in 1927. The attacks of lymphangitis recurred at intervals of a fortnight or a month resulting in elephantoid swelling of the leg and foot. In 1932, the circumference of the left calf was 22 inches, while the right was 13½ inches. At this stage the patient underwent an operation for amputation of the left leg as a measure of cure of lymphangitis and elephantiasis. The patient remained free from attacks of lymphangitis till 1936 when the right



Photograph of the patient K. G. taken on 30-7-42.

leg was affected for the first time. These attacks have been recurring since in the right leg once a year and as a result the leg has developed a moderate elephantiasis. In October 1941 and again in July 1942 lymphangitis appeared in the stump of the left leg producing gradual swelling of the stump. (see photograph).

From the above it is seen that amputation has not conferred any benefit on the patient, except relieving him of the weight of the elephantoid tissue of the leg. The onset of elephantiasis of the stump of the left leg and the recurrence of lymphangitis would show that filariasis of a limb has not been cured by amputation.

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SYPHILIS AND THE SEROLOGICAL TESTS

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It has been my experience and also that of some of my colleagues that often the Kahn or Wassermann test of the blood is declared as positive in a patient when it is least expected from his history and physical examination. During medical training, it has been repeatedly impressed on our minds not to believe in a negative history in the face of a positive serological test. As regards venereal disease it is said that neither a prince nor a pauper should be considered as exempt from it. We are also taught that in the absence of evidence or history of acquired syphilis, a serologically-positive case may be due to inherited syphilis. We are encouraged to put down the equation, positive Wassermann or Kahn equals syphilis.

In the light of my limited experience, I would consider such a dogmatic statement as nothing but medical despotism. Though the above equation is right, perhaps, in most cases, I firmly believe that there are some cases where the equation does not hold good. By undue confidence in the serological test we are doing much wrong to a number of innocent persons by stamping them as syphilitic. It should be clearly understood that the Wassermann or Kahn test is not a specific test in the immunological sense. I mean thereby that the antigen employed in the test is absolutely non-specific as far as the syphilitic antibody is concerned. It has also been shown that the tests may be positive in a number of other conditions, e.g., malaria, leprosy, yaws, etc., although the tendency is to attribute some of the positive results seen in such diseases to faulty technique.

The case of a serologically-positive subject with a negative history is looked upon with greater suspicion when his malady responds to the specific 'anti-syphilitic' treatment. Then, the temptation to put him down as syphilitic is very great and my aim in writing this paper is to warn the profession against this grave injustice towards their patients. I am fully aware of the fact that the maladies of the patients giving a positive serological test for syphilis often respond surprisingly well to the so-called 'anti-syphilitic' treatment. But this should not make one believe that the disease cured by the treatment is syphilis. This conclusion is fallacious. The fallacy arises from the association of the disease with the treatment. A drug may be previously known to be specific for a particular disease, but as our knowledge widens it may be discovered later that it has a favourable effect on a number of other pathological conditions, known and unknown. So it is wrong to diagnose a disease from the drug that cures it. The therapeutic test is of a very limited value.

Though the arsenicals are effective against the treponema of syphilis, it is well known that they are also effective against the spirochaetes as a class. This is shown by their efficacy in yaws, rat-bite fever, relapsing fever, etc. It is possible that a person giving a positive serological test for syphilis may be a subject of a non-specific spirochaetal infection, since spirochaetes are common in the oral cavity, respiratory tract, and intestines. If no evidence of such an infection be found, one should remain satisfied with the bare truth that the arsenicals are effective where the serological test is positive, without deducing the presence of syphilitic infection in the subject. Such a deduction is unwarranted in the absence of a positive history or manifestation of the disease. Thus, the arsenical treatment would be more appropriately called 'anti-Kahn' or 'anti-Wassermann' treatment rather than the 'anti-syphilitic' treatment.

In support of my view, I submit the following two cases :—

Case 1.—Woman, aged 25, came under my treatment for an ulcer in the left mammary region, of about three weeks' duration. It was oval, about 2 inches by 1½ inches, with punched out margins. It started as a small weeping area which later broke down into an ulcer of the above description. Stimulant treatment for a fortnight with eusol fomentations, hypertonic saline compresses, silver nitrate touching, etc., proved to be useless. Ultra-violet irradiation with cod-liver oil dressing for another fortnight offered no prospect of healing. Syphilitic infection could not be thought of in this particular lady or her family; however, as a result of the dogmatic teaching received, a Kahn test of blood was made and found to be strongly positive. Surprisingly enough a single dose of N.A.B. caused complete healing of the ulcer in a few days. The blood of the husband and two children, one brother and one sister, was examined and found to be negative in the Kahn test, and there is no history of any treatment by courses of injection. She had two previous normal deliveries. There is no history of abortions or miscarriages; besides the serological finding and the ulcer, there is no evidence of syphilis, congenital or acquired.

Case 2.—Woman, aged 24, came under my observation because of four abortions. She had two previous normal deliveries. Blood examined by the Kahn test was found to be strongly positive. The patient was put on arsenical treatment. After a full course, the patient conceived and in due course gave birth to a healthy son. The Kahn test of the blood of the husband and two children was done and results were negative. There is no history of any treatment by courses of injections in the relations. There is nothing in the patient to suggest congenital or acquired syphilis except the serological findings and the history of abortion.

These observations do not lower the value of the serological tests. It has been found by long and wide experience that serologically-positive cases respond well to the arsenical treatment though the cause underlying this will have to be explored in cases where there is no evidence of spirochaetal infection. Apart from the medical interest, the theme of this paper, if substantiated by other observers, is more important from the sociological point of view. Serologically positive cases will not be then labelled as syphilitic unless there is some other corroborative evidence in the family or personal history of

(Concluded on opposite page)

THE PRECIPITIN TEST AND THE PRODUCTION OF PRECIPITATING SERA

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and

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A. Introduction

THE precipitin test is the only means of obtaining exact information of the feeding habits of blood-sucking insects. It is a valuable method of studying insect transmission of disease, particularly of malaria. The difficulty of producing precipitating sera, especially anti-human serum, is responsible for its restricted application in this country where workers have with few exceptions made use of sera prepared abroad. The purpose of this article is to give the essential features of the preparation of precipitating serum and of the precipitin test, and to discuss other matters intimately associated with this subject.

(Continued from previous page)

the patient or in his physical examination. Thus, a number of subjects will be saved from the stigma of syphilis.

My contentions in this paper are :—

(1) A serologically-positive case should not be considered as syphilitic unless there is some corroborative evidence in the personal or family history or in the physical examination of the subject.

(2) Response to arsenical treatment alone should not be considered as sufficient evidence to make a diagnosis of syphilis though the subject is serologically positive.

(3) The name 'anti-syphilitic' treatment is damaging to non-syphilitic sero-positive subject improving on it. The treatment should be named as 'anti-Kahn' or 'anti-Wassermann*' treatment.

[Note.—We support all attempts to keep the laboratory in its proper place as the servant and not the master of the clinician. We are in complete agreement with the author's main contention that serological findings unsupported by clinical or other evidence are of very little value. We think, however, that the history of repeated abortions in case 2 might possibly be sufficient confirmation of the serological finding, and also the ulcer which looked syphilitic in case 1. In both these cases there was clinical as well as serological evidence.]

Moreover we think that this question of 'stamping as syphilitics' and 'stigma' needs comment. We are doctors and not moralists, and we should diagnose and treat the disorders of our patients and not sit in moral judgment on them or their relatives. Even if we diagnose and treat syphilis, it may be unnecessary or inadvisable to tell the relatives or even occasionally the patient himself.

If 'much wrong' is done to 'innocent persons', it is done not by the very occasional wrong diagnosis (for the patient may benefit markedly from anti-syphilitic treatment) but by the unnecessary publicity and moral judgment which too often go with the diagnosis. These should be avoided at all costs.—EDITOR, *I. M. G.J.*

This method of determining the origin of unknown blood in insects was introduced by Uhlenhuth and his collaborators (1908). Lloyd, Napier and Smith (1925) first put this test into use in this country when they attempted to determine the preferential feeding habits of *Phlebotomus papatasi* and *P. minutus* in connection with the possible rôle they might play in the carriage of *Leishmania donovani*. Since then it has been used by a number of workers for detecting the sources of unknown blood in anopheline mosquitoes.

The principle of this test is that when clear serum extracted from dried blood from the stomach of insects is brought into contact with a series of sera containing precipitins for blood of the possible animal sources, a precipitation or flocculation occurs in the specimen in which the blood and antiserum are homologous. At present the ring test of Fornet and Müller (1910) is universally applied for the detection of the precipitation.

B. The production of precipitating sera

Selection of animal.—Though rabbits are universally employed in America and Europe for this purpose, Sutherland (1910) in this country used fowls for preparing antisera as they are cheaper and are more readily available. Being guided by the report of Culbertson (1935) on the precipitin response of breeds of rabbits, we selected Belgian rabbits and found them to be quite satisfactory. The quantity of serum recovered from a fowl is too small and a high mortality among the experimented birds is generally experienced, a fact which was also pointed out by Johnson and Rawson (1927).

The selected animal is injected with the blood serum of the animal for which precipitins are required.

Dosage of the serum given.—Although Nuttall (1904) and other workers had failed to obtain antiserum after a single injection of serum, Hektoen (1914) succeeded in obtaining the desired result after one injection of a large quantity. Moreover, according to him, this so-called rapid method yields more reliable results with the serum of a large number of animals, except man, in which case repeated injections produce better results. For the successful production of anti-human serum, therefore, repeated injections are necessary and the process of immunization practised by different workers is more or less the same, differing only in minor details.

Sutherland and Mitra (1914) suggested 3 injections of the human serum totalling 25 c.cm., the animal's blood being withdrawn 12 days after the last injection. Subsequently they recommended a total dose of 12 c.cm. given twice. Bull and King (1923) gave a series of 4 injections of 5 c.cm. of the serum on alternate days. The dosage employed by Johnson and Rawson (*loc. cit.*) varied from 1 c.cm. to 10 c.cm. given mostly by the intraperitoneal route, and the total quantity of serum necessary to immunize a fowl was 41 c.cm.

It will thus be seen that a great majority of workers have adopted the introduction of a large quantity of serum for immunizing an animal. As it is not an easy matter to obtain human blood in bulk, we were obliged to turn our attention to the study of the effects of repeated injections of a minute quantity, and we believe this method has proved successful. 4.2 c.cm. and sometimes less was the total quantity of serum necessary to immunize a rabbit.

The injections should be given in the marginal ear vein of the rabbits and the dosage employed in fractional quantities is 0.1 c.cm. daily during the first week, 0.2 c.cm. during the second week and 0.3 c.cm. during the third week. During the third week the blood should be examined frequently to gauge the degree of precipitating action developed by the animal, as further injections of the antigen should be discontinued as soon as the maximum titre is reached. If injections are continued without interruption, it may lead to the total disappearance of the precipitins (Nuttall, *loc. cit.*), or it may lead to the production of strong heterologous antibodies in addition to homologous ones.

If the strength of the serum does not conform to the standard (*see later*), a further course of injections of 0.4 c.cm. daily may be given during the fourth week.

During the period of immunization, the animals should be given plenty of carrots; lettuce and cabbage should be withheld as the latter are thought to be responsible for the turbidity of the serum.

The antibody response of 26 Belgian rabbits which all received the antigen in fractional doses against human and ox blood is shown in table I. It may be mentioned here that a large majority of these animals had previously been used for bacteriological, protozoological or pharmacological experiments and were re-used by us after a lapse of two to four months.

TABLE I

Showing antibody response in Belgian rabbits

Antigen used	Total number of rabbits used	Sexes of animals	Nature of reaction good	Reaction bad and rejected
Human blood serum.	23	Male 21 Female 2	10 1	11 1
Ox blood serum	3	Male 3	1	2
Blood serum digested with trypsin.	2	Male 2	0	2

Season and precipitin production.—The work was started during the cold weather when a very large percentage of animals gave a satisfactory response, but when it was continued

during the summer, the response was extremely bad. During the next cold weather again satisfactory results were obtained. No definite statement can however be made on the relationship between antibody response and season, but it appears that this work should be undertaken during the winter in preference to other seasons in the tropics.

Effect of re-inoculation with blood serum.—On the basis of the observations made by Dean and Webb (1928), it may be stated that a single injection of horse serum given in a previously sensitized rabbit leads to a secondary response which is of a different character from the initial one. Within a short time the titre of the antibody is forced up to a higher level than that which followed the primary stimulus. In regard to the secondary response of precipitins, some interesting observations were made. When 6 rabbits were immunized with human serum by repeated injections in fractional doses, there was the appearance of strong homologous and, in some animals, of weak heterologous precipitins also. After the lapse of some time when the specific antibodies had become considerably weaker, a second course of injections of the same antigen caused a rise in the titre of the specific antibodies and, in addition to this, heterologous antibodies made their appearance in all the animals, and this occurred even in those in which no trace of heterologous precipitins had been detected after the primary course of stimuli. The titre of the heterologous antibodies were nearly as strong as that of the homologous ones.

This explains the circumstances in which Bull and King (*loc. cit.*) obtained dual reactions with anti-human serum.

Effect of non-specific stimulation.—In the case of immunization by bacteria, a non-specific stimulation of the antibody-producing organs in a previously immunized animal under certain conditions results in reappearance of the antibodies, which is often referred to as an 'anamnesic reaction'. In this connection it may be stated that attempts on our part to stimulate the antibody-forming apparatus in rabbits, previously immunized with human blood, by non-specific stimuli, *e.g.*, egg albumin, have met with failure. Several injections of a saline solution of egg albumin were given into the vein at the time when the specific antibodies had considerably declined, without any increase in precipitin being observed.

Heredity and precipitin production.—It is commonly supposed that the disposition to respond to stimulation by animal or human blood is inherent in the animal itself. This was tested in rabbits, some of which had responded well after the first series of injections. After a lapse of some time, when on testing their blood, no trace of specific antibodies could be detected, they were subjected to another course of injections of the same antigen as previously. The animals during the interval between the primary and secondary courses of injections had

either slightly gained in weight or had maintained more or less constant weight. The nature of the response is indicated in table II.

preceding the beginning of the second and subsequent series of injections. In this way these authors were able to obtain more than 200 c.cm.

TABLE II

Effect of secondary stimuli after an interval of some months in previously immunized rabbits

Rabbit numbers	Antigen used	Dosage during secondary stimulation	Interval between primary and secondary stimulation	Initial response	Present response
1	Human blood	0.2 c.cm. daily for 7 days.	6 months	Good	Good
2	"	"	"	"	"
4	"	"	"	"	"
5	Cattle " blood	"	4 months	Bad	Bad
6	"	"	"	Good	Good
				Dual reactions against cattle and man nearly overlapping each other.	The same as after primary stimulation.

It is apparent that the response of the above animals to primary and secondary stimuli was identical and it seems possible that the antibody production in an animal is to a great extent dependent on the character of its internal mechanism which is inherited.

Collection of blood.—The animal should be starved for about 18 hours before the blood is collected, and an hour before the blood is withdrawn it should be allowed to drink plenty of water, the object being to obtain not only clear but also a large quantity of the serum.

The practice usually followed in drawing out the blood from an immunized animal is to open the carotid artery and to bleed it to death.

Instead of collecting all the blood at one time, we advocate the withdrawal of 20 c.cm. of heart blood at intervals of 4 to 5 days as long as the potency of the serum has not sufficiently deteriorated to warrant its rejection. Accidental deaths from heart puncture are not very common, though they do at times occur. In this way we have been able to recover a much larger quantity of serum than would have been possible if a single collection had been made by opening the carotid artery.

Further if it is proved that the immunity response is dependent on the mechanism of the antibody-producing organs, which according to our findings is inherent in the animal, it therefore pays to use a satisfactory animal more than once.

Bull and King (*loc. cit.*) also followed the same procedure for collecting blood from immunized animals. From 9 to 12 days after the last injection, about 50 c.cm. of blood was collected from the same rabbit by cardiac puncture. Two days later a second bleeding of the same amount was made. After a rest of about a week, the whole process was repeated. In many instances rabbits were given as many as five series of injections and were bled twice following each series. Anaphylactic reactions were avoided by giving a preliminary injection of 1 c.cm. of the serum subcutaneously the day

of potent precipitating serum from each rabbit, though they admitted that they were unable to obtain a potent anti-human serum.

As far as possible the syringe should be dry and this can be effected by washing with ether. For separating the serum from the clot, test-tubes are preferable to flasks.

The serum should be preserved in 1 c.cm. sealed ampoules in cold storage.

Keeping properties of serum.—The precipitins are fairly stable bodies and if stored in a refrigerator will keep for a long time. On the keeping properties of anti-human precipitating serum, some interesting observations were made. From the response of rabbits to the injections of human serum, they were placed under two categories, 'good' and 'bad', the serum of the former attaining a fairly high titre in between 12 and 16 days, whereas in the latter group of animals a reasonably high titre of the precipitins was not attained till 21 days. Even after one year's storage, serum from 'good' animals was still active while in three months the potency of the serum from 'bad' animals had considerably declined.

It is therefore thought proper to suggest that for long-continued preservation the serum of 'good' animals should be chosen while the serum of 'bad' animals should be used up as quickly as possible.

The question whether or not a preservative should be added to the serum before it is stored in sealed tubes, can be answered by stating that the development of contamination has not been found to lower markedly the titre of the serum.

Hæmolysis.—When blood from an immunized animal is collected in a tube, the serum that separates out within the first 24 hours is generally a clear fluid. If further attempts are made to collect the rest of the serum that separates on the second and third days, it is likely to be blood-tinged on account of hæmolysis. Such blood-tinged serum is generally considered to be useless, as the white ring under such conditions is supposed to be inconspicuous. This,

however, is contrary to our experience. The reaction obtained with coloured serum is as clearly defined as with clear serum. It should be emphasized that red blood cells should be completely excluded by centrifugalization from any serum, be it tinged or clear, as their presence will cause a varying amount of turbidity when such antiserum comes in contact with the antigen.

Testing precipitating serum.—For the purpose of testing the serum the ring test of Fornet and Müller (1914) is employed. The antigen is first introduced by means of a capillary pipette into a small glass tube having a diameter of 3 to 4 mm. and thereafter the precipitating serum is cautiously run along the wall of the tube by means of a separate pipette. A 'ring' forms at the site of contact between the antigen and the serum.

The potency of the precipitating serum is judged merely by the reaction time, i.e., the earliest time within which a well-defined ring appears. Its character is judged by testing with both homologous and heterologous antigens. The standard to discriminate useful from useless serum is considered from the following:—

Precipitating serum + Homologous antigen diluted 1 : 1,000 = Definite ring within 2 to 3 minutes.

Precipitating serum + Heterologous antigen diluted 1 : 500 = No reaction within 5 minutes.

In all our tests the above standard representing the character of a 'useful' serum has been strictly followed.

A precipitating serum may be either specific or non-specific. These terms are, however, relative because a serum will often yield a quick specific and a delayed non-specific reaction. When both specific and non-specific reactions appear with only a short interval between them, the serum is as a rule useless for practical purposes unless it is found that when the precipitating serum has been diluted with salt solution, the interval between the two reactions is considerably increased, but the diluted serum must still yield the characteristic reaction with the homologous antigen within 2 to 3 minutes.

Sutherland and Mitra (*loc. cit.*) define their antisera as being potent if a reaction is obtained in 1 or 2 minutes with the homologous serum diluted 1 in 1,000 and specific if there is no reaction with a heterologous serum in 20 minutes. Our standard for serum to be used for entomological purposes is roughly the same. Even if the serum is not specific, the delayed reaction time allowed with heterologous serum completely excludes the possibility of any misleading reaction being obtained.

In order to determine to what extent the bulk of the precipitating serum can be increased by dilution with normal salt solution without reduction of its potency below the standard laid down above, the serum diluted 1 : 5, 1 : 10, etc., should be tested. Thus if a sample of anti-human precipitating serum diluted 1 : 10 when

brought into contact with the homologous antigen diluted 1 : 1,000 still yields the characteristic reaction within the specified time, i.e., 2 minutes, this indicates that this sample will permit of dilution 10 times. The object is to economize in material. Emphasis is laid on the point that for practical tests of mosquito blood, the quantity of which is unknown, in order to minimize the chances of 'missed' reactions the precipitating serum should never be diluted to the maximum limit; therefore fairly strong though diluted serum should always be preferred. It is further emphasized that the serum should always be preserved as such, and that any dilution necessary for economy should always be done just before use. Diluted serum can be used for only one day after dilution and only if cold stored.

C. Stomach meal preparations

Method of preparation.—For this purpose only those insects should be chosen which have recently fed on blood and in which its presence in the stomach can be detected from outside. As soon as the specimen has been identified and killed, the blood meal should be pressed out by crushing the abdomen on a piece of filter paper with a solid glass or metal rod. The expressed blood is soon absorbed by the filter paper. All traces of blood should be removed from the glass rod by wiping before the next specimen is dealt with. Each 'blood spot' on the filter paper should bear the same number as the insect. The filter papers are stored in a small covered jar, preferably in a dark cool place, and when a large number have been collected, they are to be tested for the determination of the sources of their blood meals.

Deterioration.—For convenience, preparations on filter paper are usually stored in a dry condition for some time before they are subjected to precipitin tests. It would therefore be interesting to know if such a practice of delaying the examination has any effect on the reaction. In order to study this matter, human blood meals of *Aedes aegypti* were prepared on filter paper and stored inside a drawer. The results are shown in table III.

Effect of digestion.—Blood-feeding insects like Glossina and Chrysops (Wigglesworth, 1929, 1931) have proteolytic enzymes of the tryptic type in their mid-gut. The longer the process of digestion is allowed to continue, the more the blood will be acted upon by the enzyme. The chances of detecting the origin of blood in their alimentary canal thus become correspondingly minimized.

The progressive effect of digestion of the ingested blood in mosquitoes on the precipitin test was therefore studied and the results are incorporated in table IV. King and Bull (1923) in preliminary experiments found that blood which had been ingested more than from 12 to 18 hours did not give satisfactory reactions, while Davis and Philip (1931) obtained definite

TABLE III

Results showing the deterioration of freshly ingested blood

Total number of specimens tested	Interval between feeding and preparation	Number of positive findings	Per cent of + findings	Time of the year when examinations were made	Interval between preparation of materials and examination	REMARKS
57	Killed immediately after feeding.	56	98.24	September	15 days	The negative specimens were re-examined.
12	"	12	100.00	"	17 days	
22	"	20	90.9	"	19 days	

reactions with specimens of experimentally fed insects prepared 24 hours after feeding, but no reaction when prepared after 48 hours.

Drying of mosquitoes.—Bull and King (*loc. cit.*) found that when blood was allowed to dry in the mosquito, it underwent disintegration and a

TABLE IV

Effect of digestion on precipitin reaction in the laboratory and in cool surroundings

Number of mosquitoes tested	Period of digestion	Interval between preparation and test	Number of positive reactions	Percentage of positive tests	REMARKS
78	Within 1 hour	24 hours	78	100.0	These observations were carried out in the laboratory during July, August and September, temperature varying from 84° to 90°F.
50	1 hour	15 days	48	96.0	
80	12 hours	1 day	78	97.5	
55	18 hours	The same day	54	98.18	
50	18 hours	4 days	46	92.0	
67	20 hours	1 day	64	92.52	
67	20 hours	10 days	59	85.07	
63	22 hours	12 days	52	82.5	
48	24 hours	11 days	35	72.9	
38	28 hours	24 hours	29	76.3	
62	28 hours	24 hours	49	79.03	
90	28 hours	10 days	43	47.7	
32	44 hours	The same day	0	0.0	
73	48 hours	"	0	0.0	
92	Within 1 hour	12 hours	92	100.0	Mosquitoes were fed and kept in a cool room where the temperature varied from 76° to 78°F.
33	"	24 hours	33	100.0	
44	12 hours	11 days	44	100.0	
45	48 hours	10 days	27	60.0	
20	72 hours	The same day	5	25.0	

Although Bull and Root (1923), Johnson and Rawson (*loc. cit.*) and many others hold the view that a filter paper preparation of stomach blood is fairly stable and can be preserved indefinitely, our results indicate that with keeping, gradual disintegration of blood takes place, and that the keeping properties of digested blood is poorer than that of freshly ingested specimens. Specimens in which digestion has advanced considerably should be examined as soon after preparation as possible.

The process of digestion is considerably delayed in cold surroundings, and for this reason Christophers, Sinton and Covell (1939) have advised the transportation of mosquitoes from the field to the laboratory in tubes kept inside a thermos flask containing ice. In Calcutta the mosquitoes are better killed immediately after capture, as then mosquitoes remain sufficiently soft to allow good filter paper preparations to be made for at least 6 hours after their death.

satisfactory reaction was not obtained. To study the conditions under which dried mosquitoes can be utilized for this purpose, the specimens after feeding were killed and kept in test-tubes for examination at a later date. It will be noticed from the results tabulated below (*vide* table V) that, though dried mosquitoes, when examined within 24 hours, offer quite a reasonable chance of detecting the source of their blood meals, any further storage will allow a rapid disintegration of the ingested blood.

D. The performance of the test

Attention has already been drawn to the fact that the principle involved in practical tests is to bring the antigen and the precipitating serum in actual contact without allowing the two to mix with each other. Positive reactions are indicated by the appearance of a white ring within the specified time at the site of contact. As dual reactions with precipitating sera and

TABLE V

Results of examination of dried mosquitoes

			Interval between blood feed and killing	When tested after killing	Total num- ber used	Number showing + reaction	Percentage of positive tests
<i>Aedes aegypti</i>	Soon after	24 hours	22	21	95.4
"	"	..	"	11 days	1	0	0.0
"	"	..	5 hours	24 hours	73	70	95.8
"	"	..	5 hours	6 days	52	23	44.2
<i>Culex fatigans</i>	5 hours	6 days	7	0	0.0
<i>Armigeres obturbans</i>	5 hours	6 days	7	0	0.0

even three reactions with anti-human serum (man, dog and cattle) are common, the time limit must be strictly enforced in order to avoid overlapping of any of these reactions. The standardization of the serum extracted from the dried blood is impossible, and it is for this reason that we advocate that use of fairly strong precipitating serum though it may be diluted.

The two methods which are commonly applied for testing unknown blood of insects are (1) separate examination in serological tubes and (2) examination *en masse*.

The first is well known and was extensively used till Rice and Barber (1935) advanced an improved method which allows examination of a large number of specimens within a short space of time. It will not therefore be out of place to give a short résumé of *Rice and Barber's technique*. The essential apparatus required for this test are the following:—

(1) A metal tray divided into a number of compartments, each compartment measuring 5 cm. × 3 cm., being 2 mm. wide at the bottom and considerably wider at the top; these are used for soaking the dried blood preparations separately in salt solution.

(2) A mixture containing sodium chloride, glycerine, phenol and distilled water for diluting the precipitating serum according to its titre.

(3) A number of capillary tubes, each about 6.5 cm. long and 2 mm. inside diameter. Five such tubes, sealed between two glass slides, are termed a 'card'.

(4) Five small pots for holding the diluted antisera prepared against five different types of animals.

(5) The procedure adopted is to dip the tubes placed on the 'card' in one compartment of the tray in which the extract of the dried blood in salt solution has been prepared.

All the five tubes are quickly filled up to variable lengths with the same type of antigen. The ends of the tubes are then touched to a layer of wet absorbent cotton-wool to draw out a part of the antigen. The tubes are next dipped into the dishes containing five different types of precipitating sera, which at once rise into the tubes. The pots containing the antisera are placed in a line at such a distance from each other that, when the card is lowered on the pots,

the five tubes will draw in fluid separately from the five pots; thus the different tubes will contain the five different types of antisera.

The zonal reaction at the contact between the antigen and the precipitating serum should be read up to 20 minutes.

This method of testing unknown blood *en masse* no doubt presents certain definite advantages. It economizes time and also precipitating serum. It cannot, however, be considered as perfect and certain deficiencies which are experienced in its practical application are here pointed out.

—Stomach meal preparations of mosquitoes prepared by crushing the insect on filter paper often cover quite a large area, and these spots may often have to be cut up into smaller bits in order to accommodate them in a tray having a width of 2 mm. at the bottom, especially when only a few drops of salt solution are required to extract serum from the dried blood. In the tropics the loss of fluid due to evaporation from trays, 5 cm. × 3 cm., unless they are kept covered, is great. The cleaning of capillary tubes and their washing while still fixed to the glass card cannot be conveniently performed. In order to allow the capillary action to continue after the tubes have been loaded with the antigen, which is the extracted serum in this instance, a small amount of the contents must be expelled which, as has been advised by Rice and Barber (*loc. cit.*), should be done by touching the ends of the tubes with wet cotton-wool. The fluid is so quickly drawn out from tubes having 2 mm. inside diameter, that one must be extremely careful to prevent their complete emptying. In actual practice such accidents have often occurred in our hands, necessitating a repetition of the whole process. Though the authors advise mere contact of the ends of the tubes with the fluids, both the antigens and the precipitating sera, in practice one really dips the ends of the tubes in the fluid which necessarily adheres to the side. The danger of contamination of the precipitating serum cannot be eliminated by merely touching the end of the tube with wet cotton-wool.

It is possible to remedy the above drawbacks in Rice and Barber's method and for this purpose the present authors have adopted a modified

technique, the details of which are given below :—

Authors' technique

1. Dilution of the precipitating serum.

In order to minimize the expenditure of the serum, the highest dilution in which it reacts with the homologous antigen within the specified period must first be determined so that the bulk of the serum can be proportionately increased by diluting with salt solution. Weak sera must be used in the concentrated form. The estimated amount that is likely to be consumed in the course of a day should be prepared.

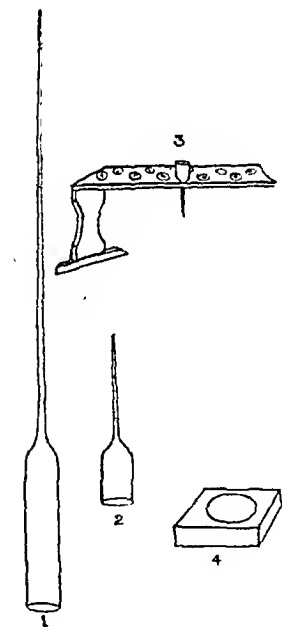
It is essential that the serum must be tested immediately before it is actually put into use.

2. Only the actual blood spots are to be cut out from the filter paper. These are now allowed to soak in normal saline solution for two hours in separate test-tubes in a rack, the latter being shaken from time to time. The solutions are then poured into separate hollow glass blocks of small size just before use. The glass blocks are arranged in a regular order so that their labelling can be avoided.

3. Antisera, either concentrated or diluted, are poured also into separate glass blocks (figure 4), and these should be kept covered.

4. Testing tubes are specially prepared from Pasteur's capillary pipettes (figure 1). A large portion of the upper part and much of the capillary part except the first $1\frac{1}{2}$ to 2 inches are cut off, and the sharp edges are rounded to avoid accident (figure 2).

5. These tubes are left in ordinary tap water or distilled water, if available, and before they are used, the water is expelled by jerking. Even a minute column of water, especially in the narrow end, will interfere with the capillary action.



1. Pasteur's pipette.
2. Testing tube.
3. Wooden rack for placing testing tubes when loaded with the antigen and the precipitating serum.
4. Hollow glass block.

6. The actual test now begins. Immediately after the water has been expelled from the tube, the capillary end is first dipped in the mosquito blood solution, when the fluid at once rushes up to a distance depending on the internal diameter of the tube. This end is now quickly drawn through a piece of towel held in the left hand to wipe out the fluid from the outside of the tube. It is now touched to a piece of filter paper and

nearly half of the contents are allowed to run out. The capillary end is next dipped in the precipitating serum which is at once drawn inside. The tube is now put into a specially prepared wooden rack with suitable holes (figure 3) to accommodate the ends of the tubes and with sufficient height that the capillary end of the tube when put in the rack does not touch the base. In this way 50 tubes are loaded; this will take not more than 5 minutes. Their reading should not be postponed later than 5 minutes, and this can best be done by holding the rack and examining the tubes against a black cardboard. If the room is not well lighted, suitable arrangements for artificial light should be made. Only positive reactions are entered in the book. Occasionally a closer scrutiny is necessary in which case the particular tube will have to be taken out. When the test does not give any conclusive result, the particular specimen may have to be re-examined.

So far only one antiserum has been used, and the examinations have to be repeated with other antisera. In this way the examination of 50 samples at a time are performed with the different antisera.

It is necessary to mention that in handling the loaded tubes a little shaking does not disturb their contents.

If the capillary end of the tube is wide, the lower meniscus of the fluid may project outside. This can be easily obviated by using pipettes which have fine capillary ends about 1 mm. in diameter. Too fine capillary tubes should never be used, as it is difficult properly to recognize the white ring.

Advantages of the method.—In order to assess the possible advantages of the above method, one has to judge it from the viewpoint of its practical application. If a large number of antisera have to be used, Rice and Barber's method has definite advantages, but when the number of animals against which the tests have to be performed is small, the authors are of the opinion that the new technique outlined above is particularly convenient and easy to apply.

In malarial entomology in India it should be emphasized that the use of two sera only, anti-cattle and anti-human sera, will generally serve all practical purposes. In Bombay, tests of the stomach blood of anopheles made by Barber and Rice (1938) failed to indicate any mosquito having fed on the pig. They used 5 different antisera against man, horse, pig, sheep and cow and their results showed that out of 1,101 positive tests, 0.5 per cent had fed on the sheep and 1 per cent on the horse, the rest on man and cattle. In the case of culicines, 2 out of 111 or nearly 2 per cent had fed on the horse and none on the pig and the sheep. Russell and Jacob (1939) reported from the Madras Presidency that out of a total of 730 tests performed with many species of anopheles, only 0.6 per cent were positive for sheep and the rest gave reactions against man and cow and none

against dog and pig. In their report on the food preferences of different anopheles in Delhi, Afridi and his collaborators (1939) stated that out of 7,249 specimens of anopheles of 4 species, those which had fed exclusively on pig, dog and sheep only numbered 1, 1, and 2, respectively, the rest of the positive tests were obtained against cow, horse and man. In Jeypore Hills nearly 3.6 per cent of anopheles out of a total of 165 were noticed by Senior White (1938) to have fed on goat, and the rest on man and cow. Senior White (*loc. cit.*) makes the significant remark that pigsties are not attractive to Indian anopheles. Out of 1,771 stomach-meal preparations of mosquitoes collected in Wynaad, Southern India, which yielded positive results, only one was found to have fed on both horse and man, and the rest on man and cattle (Covell and Harbhagwan, 1939).

The data recorded above indicate that the precipitin tests for the blood of man and cattle are applicable all over India and only in certain areas may it be necessary to test for the blood of goats or horses. This means that the saving of time made by following the technique of Rice and Barber will be very little.

The method of recording results.—Lloyd, Napier and Smith (*loc. cit.*), who first put this test into use in this country, expressed their results from a general consideration of the attraction of sandflies to different hosts. Ramsay, Chandra and Lamprell (1936), on the other hand, took into consideration the total number of mosquitoes which were subjected to precipitin tests, a procedure which was copied subsequently by Roy, Chandra and Siddons (1938). Lamprell (1936), in a critical examination of food preference of mosquitoes of the orient, compared his own findings with those recorded by Walch (1932)*, who had ignored the total number of specimens which had been subjected to precipitin tests and had included only those which yielded positive tests. In this way the basic data accepted for comparison by Lamprell (*loc. cit.*) were not correct.

In order to maintain uniformity, it is suggested that the preferential feeding habits should be indicated not from the total number subjected to precipitin tests but from those which give positive reactions against different animals, a practice followed by the large majority of workers.

Summary and conclusions

1. Belgian rabbits have been successfully used for producing precipitating sera.

2. Injections of the antigen (animal's serum) in fractional doses have been tried with good results.

3. The relation between season and precipitin production has been studied.

* Walch (*loc. cit.*) has not mentioned the total number of mosquitoes which were subjected to precipitin tests but only those which yielded positive results.

4. Reinoculation with serum leads to the production of strong heterologous precipitins and attempts to stimulate precipitin producing organs in a previously immunized animal with egg albumin have failed.

5. The results obtained after a second course of injections have been noticed to be identical with those obtained in the same animal after the primary course, suggesting a strong hereditary disposition on the part of the animals to produce precipitins.

6. Repeated collections of blood by cardiac puncture of satisfactory animals will make it possible to obtain a larger quantity of high titre serum than when the animal has been bled to death.

7. The results of studies on the keeping properties of the serum of two types of animals, 'good' and 'bad', as judged from their precipitin production, indicate that the titre of the first type of serum remains unaffected on preservation in cold for a year, while that of the second type soon deteriorates.

8. Precipitating serum when tinged with blood due to hæmolysis will yield the same results as clear samples.

9. Deterioration of stomach-meal preparations and the effects of digestion and drying of mosquitoes on the precipitin reaction have been studied.

10. A new technique for performing this test has been suggested and it is thought to be particularly useful when the number of precipitating sera to be used is small.

11. A suggestion has been made that in future in recording results the calculation should be made only on the basis of positive tests obtained.

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(Concluded on opposite page)

VARIATIONS IN THE RADIOSENSITIVITY OF CELLS AND THEIR THERAPEUTICAL SIGNIFICANCE

By DOZENT DR. GEORGE POLITZER

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In order to determine the most suitable dosage for the treatment of the different diseases, the radiosensitivity of normal and diseased tissues has long been studied. The authors of even the first textbooks of radiotherapy tried to range the normal and diseased tissues according to their radiosensitivity. After the first World War, efforts were made to fit the carcinomas and sarcomas into this scheme, but soon it became apparent that there are carcinomas and sarcomas of different sensitivity; this involved further investigations to trace the origin of these differences with the object of foretelling the radiosensitivity of a tumour from its histological features revealed by biopsies, and of fixing the plan of the treatment according to these findings. The most remarkable attempt of this kind was made by Borak.

Borak presumes that the radiosensitivity of a tumour depends on its histological features. The sensitivity of a tumour, he presumes, never exceeds the sensitivity of the tissue from which it derives, and the sensitivity of a tumour will increase with its differentiation from its matrix. It may be difficult to utilize this second 'rule' in practice, as the pathologists still differ rather in their views on maturity or immaturity of a tumour. But however this question may be decided in future, it is clear that the main presumption underlying the whole scheme is the idea that the radiosensitivity of a tumour depends above all on its histological structure.

Although every attempt to guide the radiologists in the treatment of malignant tumours is

most welcome, the scheme of Borak fails to consider the variations and changes in the radiosensitivity of tissues due to extraneous influences or to different phases of cell-life.

The experiments and observations on this important question are dispersed over many journals and periodicals often not available, so it seems worth while to collect the more important of them, and to draw some conclusions for therapeutic purposes.

G. Schwarz examined the influence of mustard oil on the radiosensitivity of the skin. He found that application of mustard oil increases the radiosensitivity; the increase depends on the time interval between the application of the mustard oil and the irradiation. The increase of the radiosensitivity is most pronounced soon after the application of the mustard oil and it progressively decreases later. This experiment of Schwarz (Holthusen, 1921) proves a temporary sensitization of the skin by mustard oil application.

Alberti and Politzer examined the action of x-rays on the cornea of salamander-larvæ. After the application of 200 R. filtered through 1 mm. of aluminium, the frequency of cell division diminished rapidly, and after 6 hours the cells of the cornea showed no division. Then follows an interval of 3 days' duration, during which no cell division takes place. After this interval cell division reappears and increases quickly and reaches normal after about 9 days. The authors divide the whole action into three periods, the primary effect (till the subsidence of the mitosis), the interval and the secondary effect. In four other series of experiments a second dose of the same strength has been administered after 3 hours (series A), 18 hours (series B), 4 days (series C) and 9 days (series D). If the second dose is given during the primary effect or the interval (series A and B) the effect as a whole is the same as if the sum of both doses had been given at the same sitting. But if the second dose is given at the beginning of the secondary effect (series C) or even more if given during the height of the secondary effect (series D) the total effect does not correspond to the sum of the individual doses, but to a multiple of them. This proves that subsequent to an x-ray treatment, an increase of the radiosensitivity of the tissues takes place which reaches its summit after some time. Most probably the sensitivity returns later to the previous level or it may sink even below the previous level, but these latter presumptions could not be proved in our experiments.

The experiments of Schwarz (Holthusen, *loc. cit.*) and of Alberti and Politzer concerned changes of the radiosensitivity of tissues produced by extraneous influences; we here consider the variations in radiosensitivity occurring under physiological conditions.

In nearly every tissue some dividing cells are always to be found and it would be of interest to know if the radiosensitivity of a tissue depends

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also in the 'B' fraction of the bile which comes from the gall bladder during the Lyon-Meltzer test. The very large number of parasites present in the 'B' fraction cannot but convince one of the fact that the gall bladder acts as a reservoir where they multiply and grow. The number decreases rather markedly in the 'D' bile and in the duodenal content.

These facts indicate that the parasite is always present in the duodenum and the gall bladder when the individual is passing the cysts in his stools. The association of this finding with the small blood clots and a few pus cells gives evidence of the fact that there is a constant irritation and catarrhal inflammation of portions of the duodenal mucosa, and the same is true of the gall bladder, where however the only sign of irritation is an excessive quantity of mucus which appears in flakes entangling the parasites. The symptoms vary according to the severity of this irritation and inflammation and to the site where it is most marked. In cases of group I, the duodenum is the site of a mild catarrhal inflammation and hence the signs simulate duodenal ulcer. In group II the constant irritation of the duodenum and the gall bladder causes a vague pain and sometimes a colic which occasionally resembles a mild attack of gall bladder colic, the gall bladder region becoming tender on palpation. In the cases of group III the infection spreads to the ileum and thus causes diarrhoea. The spontaneous amelioration of the symptoms of these cases for short periods represents an attempt on the part of the body to overcome or limit the infection.

The treatments which have been found effective are as follows :—

(1) Stovarsol gr. iv given by mouth twice daily for 10 days, or (2) N.A.B. .45 gm. given intravenously—1 injection, or (3) atebirin 0.1 gm. given thrice daily by mouth for 5 days, or (4) a course of bismuth injections totalling 2 gm.

A few case reports are quoted to illustrate the above statements :—

Case 1.—R. M., aged 35 years, came to the hospital with the following complaints :—

(a) Pain in the upper abdomen specially marked about 3 to 4 hours after food—duration several years. The pain is relieved by Maclean's powder and pain-free periods occur.

(b) Constipation alternating with diarrhoea for several years.

(c) For about a month he has had diarrhoea with mucus in his stools and lost about 10 pounds in weight. He felt weak and had a disinclination for work.

(d) 'Acidity' for the last 3 or 4 years.

His right hypochondrium was tender on palpation; colon not thickened.

A fractional test meal showed a low acid curve; examination of stools revealed cysts of *Giardia intestinalis* in large number.

Lyon-Meltzer test revealed the following :—

(a) 'D' bile showed excess of mucus and small blood clots. Under the microscope a fair number of the vegetative form of *Giardia intestinalis* were found with occasional pus cells and R.B.C. Duodenal corpuscles were present in fair number.

(b) 'B' bile was of usual viscosity with floating flakes of mucus in large number. The flakes of mucus showed very numerous vegetative forms of *Giardia*

intestinalis entangled in mucus. An occasional desquamated columnar epithelium and pus cell was seen.

The patient was advised to take stovarsol 4 grains twice daily after meals for 10 days; after about 2 weeks he was symptom free and the stools were free from the cysts.

This case has been followed up for the last 4 months and no recurrence of symptoms noted. The stool has been free from the cysts.

Case 2.—Md. S., aged 18 years, complained of vague pain in the upper abdomen and occasional colicky pain. He was exceedingly neurotic. Investigation revealed cysts of *Giardia intestinalis* in his stools. Cholecystography and barium meal examinations were done and the radiologist reported duodenitis. The fractional test meal revealed an acid curve within normal limits.

A course of stovarsol made him symptom free and he remained so for 2 months after which I lost sight of him.

Case 3.—N. M., aged 16 years, came with the following complaints :—

(a) Passing yellow-coloured urine for the last week.

(b) Yellowishness of the conjunctiva for 7 days.

(c) Vague pain in abdomen for the last 3 years.

(d) Diarrhoea off and on for the last 3 years.

(e) An attack of fever about 10 days previously.

His stools were clay-coloured and revealed the cysts of *Giardia intestinalis*. The van den Bergh reaction was biphasic.

The Lyon-Meltzer test showed a duodenal content very slightly tinged with bile and teeming with vegetative forms of *Giardia intestinalis*, and bacteria and fungi of various types together with pus cells, duodenal corpuscles and desquamated columnar epithelium.

The 'B' bile was obtained after 3 successive stimulations and revealed the vegetative form of *Giardia intestinalis*, bacteria, occasional pus cells and a few fungi.

With drainage of the bile he made a quick recovery and later was advised to take stovarsol. The stools became free from cysts.

Case 4.—K., complained of constipation and vague uneasiness in abdomen. The stools showed cysts of *Giardia intestinalis* and the patient became free from cysts and symptoms after a course of atebirin taken rather irregularly over a period of 10 days.

Summary and conclusions

(1) *Giardia intestinalis* alone is capable of producing symptoms simulating duodenal ulcer and chronic amœbiasis.

(2) The duodenal irritation and catarrhal inflammation pave the way to bacterial infection, which sometimes produces the condition known as catarrhal jaundice and predisposes to inflammation of the gall bladder and the bile passages.

(3) Evidence is obtained of the fact that organisms can ascend the bile duct and thus reach the gall bladder. This fact has a definite bearing on the route of infection in cholecystitis.

My thanks are due to Dr. R. N. Roy, medical officer, Messrs. Bird & Co., Mudidih Hospital, and the medical officers at Sendra and Loyabad for the cases.

My thanks are also due to the chief medical officer and the chief mining engineer, Messrs. Bird & Co., and F. W. Heilgers & Co.'s collieries, for permission to publish the case reports.

RECOVERY OF AGAR FROM USED MEDIA

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and

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THE unique position of agar-agar as the base for solid media can hardly be gainsaid. This substance was introduced into bacteriological technique in place of gelatin at the suggestion of Frau Hesse, the wife of W. Hesse, one of Koch's early co-workers who studied bacteria of the air and who experienced difficulties owing to the liquefaction of gelatin plates. In bacteriological literature agar-agar is first mentioned by Koch in 1882 in his paper on tuberculosis.

The difficulty of obtaining China grass (the parent body of the substance agar-agar; it grows almost exclusively in Japan) on account of the present international situation has raised its price from Rs. 3 to Rs. 35 per lb., and if the war continues much longer this will not be available at any price.

There is, we believe, a scheme for making a substitute in India, but it may be some time before this is available and meanwhile bacteriological work must go on; we therefore explored the possibility of recovering agar from used or contaminated medium. We found that this problem presented few difficulties and in a very short time we had worked out a method, which we feel may be of use to others faced with the same problem.

Collection of used agar

Used and contaminated plates and tubes of all media with an agar base were collected from different departments of this institution and washed lightly in running water from the tap. The substances from these plates and tubes (tubes being heated gently in steam or water bath) were scraped off into a suitable pot. This substance was then washed overnight by a very slow stream of water. This was done with the help of a rubber tube fitted to the tap, with the

free end just above the bottom of the sink. The water passes out through the overflow.

Melting

Next morning the washed agar is removed from the sink and collected in a clean enamel pot. This pot is then put into a steam bath and removed when the agar melts.

Purification

The melted agar is then mixed by stirring with adsorbent, prepared with bone charcoal, kaolin, chalk and water to form a thick sludge, until the temperature of this agar mixture falls to 40°C., when egg albumin (one egg per litre) is mixed with the melted substance and poured into a flask (preferably pyrex). The flask with its mouth plugged with cotton-wool is then autoclaved for 10 minutes at 15 lb. pressure. It is then removed from the autoclave and the substance is filtered through filter paper in a Buchner funnel by means of water suction pump. This filtrate is poured into a clean enamel tray, and, when it solidifies, cut into cubes. These cubes are then kept overnight in a sink under running water as described above.

Next morning the cubes are removed from the sink and kept ready for use.

This process of recovering the agar can be repeated several times, and if the agar becomes too soft as a result of repeated filtration it should be mixed with a little fresh agar.

Quantity of adsorbents to be used

	Bone charcoal	Kaolin	Chalk
For coloured agar media	10%	5%	25%
For colourless agar media	5%	5%	25%

Bone charcoal should be coarsely powdered and purified by boiling with 10 per cent hydrochloric acid and washed in water until it is free from acid.

We are deeply indebted to Dr. L. E. Napier, Director, for his encouragement and advice in carrying out this work.

A Mirror of Hospital Practice

TWO CASES OF ANTHRAX TREATED WITH 'M.&B. 693'

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Case 1.—A fourteen months' old baby, Ghasi by caste, came to my notice in the lines with an angry looking red pustule on the left arm just above the elbow with a certain amount of infiltration. Next morning the mother with the child was brought to the hospital and the following condition was observed:—

Temperature 103.4°F. The pustule has spread and the surface is covered with vesicles oozing dark-brown

serum. The base is much infiltrated. (Edema has rapidly extended to the finger tips below and to the shoulder and base of the neck above, involving the axillary, parotid, cervical and salivary glands of the affected side. The child had ceased taking the breast and was in a critical condition.

It was suspected to be a case of anthrax. Enquiry revealed that a few deaths amongst cattle have occurred recently in the garden, and these Ghasi people deal with the hides of the carcasses. A smear was taken and sent to the Central Laboratory for microscopical examination which showed the anthrax bacillus.

The article by Ghosal and Chaudhury (1942), who tried this remedy with a certain amount of success in tetanus, led me to think that it may have some

effect on anthrax as well. As serum was not available treatment with M.&B. 693 was started.

0.25 gramme of M.&B. 693 was dissolved in an ounce of water and given slowly by means of a teaspoon. Swallowing was difficult. The surface of the pustule was cauterized with pure carbolic acid and the area around it was painted with iodine liniment and was allowed to dry. Then a carbolic compress was applied. In the afternoon the temperature came down to 102.4°F. There was improvement of the œdema. The dose of M.&B. 693 was repeated.

The next morning the spread of œdema appeared to have been arrested. The surface was seen to be covered with a blackish slough surrounded by a ring of vesicles. The temperature was 101°F. The baby was seen sucking the mother's breast though not keenly. The patient had nausea which was controlled by small doses of sodium bicarbonate. 0.25 gramme M.&B. 693 dissolved in water was again given by mouth. Local treatment was as before. In the afternoon the temperature dropped to 100°F. The same dose was repeated. The baby took to her mother's breast comfortably.

The next morning the temperature was 98.4°F. Œdema had subsided from the base of the neck, the shoulder, arm and fingers. Only a necrotic area with black slough looked a bit inflamed. The oozing of serum had completely stopped. The dose was cut down and 0.125 gramme was given. In the afternoon the temperature was 97°F. The same dose was repeated.

The next morning the temperature was 97°F. The general condition of the child was quite good. The black slough was separating and granulation tissue was seen forming. M.&B. 693 by mouth was stopped and M.&B. 693 powder was applied to the ulcerated surface. This local treatment was continued for 4 days more and the child was discharged cured on the 11th October. Total quantity of M.&B. 693 given in this case was 1.25 grammes.

Case 2.—A Ghasi woman, aged about 35 years, came to the hospital on 6th October with a swelling of the whole forearm which had caused disturbed sleep on the previous night. On examination, I found an angry looking pustule on the left thumb with a brown serous exudation. The base was much infiltrated. The axillary glands were enlarged. The œdema extended up to the axillary region. The picture was exactly the same as that of the first case. The temperature was 101.4°F. Clinically the case was diagnosed as anthrax.

Treatment.—The surface was cauterized with carbolic acid and the surrounding infiltrated area was painted with liniment iodine and allowed to dry, and a carbolic compress was applied. M.&B. 693 1 gramme dissolved in water was given by mouth. The same dose was repeated at 4 hourly intervals.

Next morning the temperature was 100°F. The spread of the disease appeared to be checked. The surface was covered with a black slough. Oozing of serum stopped altogether. One gramme was given in the morning and repeated in the evening.

The next morning the temperature was 98.4°F. Œdema had somewhat subsided. There was a certain amount of swelling on the dorsum of the hand and the patient complained of slight pain over the thenar eminence. Ichthyol with belladonna and glycerine in equal parts was applied to the area. Powdered M.&B. 693 was applied to the raw surface. One gramme was given by mouth in the morning and repeated in the evening.

The next day the temperature was 97°F. and the patient was comfortable. Granulation tissue was seen forming underneath a black scab; 0.5 gramme was given by mouth and also repeated in the evening.

The next day the temperature was normal and the swelling had subsided. Oral administration of M.&B. 693 was stopped; only the powder was applied over the raw surface and continued for 3 days more. The patient was discharged cured on the 13th. Total

quantity of M.&B. 693 given by mouth in this case was 8 grammes.

Conclusion

It is too early to say from these two cases that sulphapyridine is a specific for anthrax, but I feel that it has a definite place in the treatment of anthrax and may be used as a substitute for serum. It has the advantages over serum of being devoid of risk of anaphylaxis and serum sickness, and it is easy to administer. Moreover, it is considerably less costly than the serum.

My thanks are due to Major S. J. Vere-Fox, chief medical officer, Juri Valley Medical Association, for his kind permission to publish this report, and to Mr. J. E. Danter, manager of the garden, for his keen interest and all possible help in dealing with the cases.

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A CASE OF BRONCHOGENIC CARCINOMA

By R. SUBRAMANIAM, M.B., B.S.

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THE following case is reported on account of the rarity of reports of bronchogenic carcinoma in the Indian literature. The few cases clinically diagnosed as bronchogenic carcinoma in the General Hospital, Madras, have not been confirmed either by biopsy or autopsy.

An Indian Christian male, aged 50 years, bailiff by occupation, was admitted into Dr. T. Satakopan's ward for fever of one and a half months' duration. The patient gave a history of dysentery a year ago and was treated with indigenous drugs. The patient was addicted to alcohol.

History of present illness.—Swelling over the epigastric region for the last one year. Was getting increasingly dyspnoic. Fever of intermittent nature of one and a half months' duration.

Clinical examination.—Slightly anæmic and cyanotic. No jaundice.

Respiratory system.—Trachea displaced to the right side. Rapid shallow breathing. Stony dullness over the whole of the middle and lower part of the right side of chest. Normal resonance over the right apex with cavernous breathing. Breath sounds feeble over the dull areas with a few moist sounds over the left base.

Cardio-vascular system.—Heart was slightly pushed over to the left, the left boundary being one inch outside the mid-clavicular line. The boundary on the right side could not be defined. Sounds were feeble. Pulse regular; volume and tension fair.

Alimentary system.—Liver enlarged down to the level of the umbilicus (four inches below the costal margin), very hard but not tender. No enlargement of the spleen.

Investigations.—Total white cell 14,600 per c.mm. Differential count—polymorphonuclears 80 per cent, lymphocytes 18 per cent and mononuclears 2 per cent. Stools—no amœbæ or cysts.

X-ray of chest and abdomen.—Dense opacity middle and lower part of the right side. Heart slightly pushed to the left. Trachea pulled over to the right. Dense opaque shadow in the abdomen over the liver area. Liver very much enlarged.

Pleural aspiration.—Only a small amount of blood-stained fluid aspirated. Many immature white cells seen in smears. Pathologist reported the presence of oat-celled carcinoma cells in sections made from the centrifuged deposit.

The case was admitted as one of lobar pneumonia because of the presence of fever and cavernous breathing over the right apex. The diagnosis was ruled out in the ward because of the resonance over the right apex and dullness over the base and middle lobe with feeble breath sounds. In view of the history of dysentery, amœbiasis of the liver with pneumonitis of the right base was considered, and emetine injections were given. Though there was an apparent response to the first few injections, an exploratory puncture of the pleural space and liver was done, and blood-stained material was aspirated instead of pus. This ruled out amœbic infection. At this stage it was suggested that the case was one of carcinoma of the lung with secondaries in the liver, or of primary carcinoma of the liver. A few days later when the patient expired, death was certified as due to secondary carcinoma of the liver (? primary site) as the pathologist's report was not received on the biopsy material sent for examination.

Since the body was claimed, only a partial post mortem was done by late Dr. P. Ramachandra Rao, professor of pathology, Madras Medical College.

Post-mortem findings.—No effusion in the pleural cavities. Right lung: the whole of the lower lobe consolidated. Section (plate VI, figure 1, facing page 71) showed carcinomatous infiltration of the main right bronchus and the hilar lymph nodes. The right main bronchus showed well-marked induration owing to malignant infiltration of the wall, and considerable narrowing of the lumen. The mucous surface did not show appreciable ulceration or papillary outgrowths into the lumen. The malignant infiltration extended massively in a fan-shaped manner into the lung along the bronchi, reaching right up to the pleural surface which was seen faintly bosselated due to the formation of flat sub-pleural tumour nodules. The cut surface showed a solid, firm, greyish, lobulated, irregular growth, occupying almost the entire lower lobe. The tracheo-bronchial group of glands were enlarged, infiltrated and adherent. The upper lobe showed more peribronchial infiltration. In the left lung, stray sub-pleural deposits were found in the lower lobe. Microscopical examination of sections (figures 2 and 3) made from the lung showed a papillary adenocarcinomatous infiltration of the lung. The cells were highly anaplastic with oat-shaped nuclei arranged in rosettes.

Remarks.—The condition of the lung in this case illustrates the diffuse type of bronchogenic carcinoma of the highly anaplastic infiltrating variety arising from the main bronchus in the hilar region with little tendency to the formation of polypoid masses occluding the lumen. This accounts for the absence of evidence of bronchiectasis, atelectasis and abscess formation and the corresponding clinical signs and symptoms. The absence of pulmonary fibrosis or chronic inflammatory origin in the rest of the lung in this case lends little support to the chronic irritation theory of the aetiology of bronchogenic carcinoma. The three lines of the spread of the tumour, i.e., bronchial, lymphatic and distant (hepatic), are well illustrated in this case. In the absence of complete autopsy, the presence or otherwise of secondary deposits in the brain could not be verified.

No effusion in the peritoneal cavity. Liver was very much enlarged and weighed 9 pounds. It was strewn with secondary carcinomatous deposits, discrete and conglomerate, varying in size from that of a pea to that of a lime.

The cut surface showed a finely lobulated appearance due to solid firm nodules. The intervening hepatic parenchyma showed areas of chronic venous congestion and slight bile staining. The portal group of glands were enlarged and matted.

Microscopically the section of the liver showed a papillary adeno-carcinomatous structure. The tumour cells were highly anaplastic and resembled spindle cells.

Heart: slightly bigger than normal otherwise, nil abnormal. Aorta showed atheromatous changes.

Kidneys—normal. Spleen—atrophic.

Conclusion

Ante-mortem diagnosis in this case has been facilitated by the help of the skiagram and the biopsy report on the material aspirated from the lung. In the absence of the above, the chances of missing the diagnosis would have been very great. Recent advances in diagnostic methods including bronchoscopy enable detection of a large number of cases. The patient was a city-dweller exposed to tar fumes and dust. These facts may have no significance, as it has been shown that rural workers are as much affected as the urban. Further, the absence of chronic pulmonary fibrosis rules out chronic irritation as an aetiological factor.

My thanks are due to Dr. T. Satakopan under whose care the patient was admitted, to Lieut.-Colonel G. R. McRobert, C.I.E., I.M.S., superintendent, Government General Hospital, Madras, for permitting publication of this case report, and to Dr. D. Govinda Reddy, professor of pathology, Medical College, Madras, for contributing the pathological report and photomicrographs.

A CASE OF VESICULAR MOLE WITH LIVE BIRTH

By A. CHACKO, W.M.S.

Elgin Hospital, Gaya

A MULTIPARA, aged 23 years, was admitted in labour with 30 weeks' pregnancy. The first three children were alive after normal deliveries. The fourth child was born normally but died on the 16th day of birth. The present was the fifth pregnancy. The patient gave a history of bleeding per vaginam during the fourth month of pregnancy for 16 days. She had no definite illness after that. There was no toxæmia of any kind.

On examination her general condition was below normal. She was definitely anæmic. The type of anæmia was not determined, due to lack of facilities. The urine showed no abnormality. Blood pressure was 120/80. She had a normal delivery, labour lasting about 5 hours. The child was a live female—weight 3½ pounds. The placenta was expelled in 7 minutes. There was no post-partum hæmorrhage. The placenta showed vesicular degeneration of two cotyledons. They were fairly big in size. The cotyledons that were not affected were normal in appearance. No evidence of lutein cysts was obtained by bi-manual examination. No Zondez-Aschheim test was done. The patient had a normal puerperium during which she was given treatment for anæmia. The premature baby had special nursing while in the hospital.

RUPTURE OF THE LEFT VENTRICLE— REPORT OF TWO CASES

By B. N. BALKRISHNA RAO, F.R.C.S. (Eng.)

and

C. V. NATARAJAN, M.B., D.P.H.

Kolar Gold Fields, S. India

DEATH due to rupture of the heart is uncommon, and the following two cases are worth recording :—

Case 1.—B., aged about 55 years, was alleged to have been knocked down by a horse cart at midnight, and the following afternoon the dead body was found abandoned in a field.

Post-mortem findings.—Moderately well-built female with a few abrasions on the body. The visceral and parietal pleurae were adherent at the right base, and there were a few adhesions in the left middle zone. The division of the lobes of the right lung was completely obliterated.

The pericardium was distended, but was healthy. The pericardial sac revealed an extraordinarily curious elongation into a pouch 6 centimetres long, with a clover-like division at the base into two smaller elongations laterally and to the right, one elongation being almost twice the size of the other (plate VI, figure 1, facing page 71). The pouches were filled with clotted blood. The diaphragm was strongly adherent to the base of the pericardium.

On opening the pericardial cavity, 8 ounces of dark fluid blood escaped. A small rupture (figure 1) on the anterior surface of the left ventricle, half a centimetre in length, running backwards, downwards and to the left, was noticed. It was 5 centimetres from the apex, and 2.5 centimetres from the inter-ventricular septum. The internal opening of the rupture was at the base of a papillary muscle. The surface of the heart both anteriorly and posteriorly was covered with clotted blood. The parietal surface of the pericardium was also sluggy and covered with clotted blood.

The heart measured 8.8 centimetres vertically and 8 centimetres transversely. The heart was in systole, and the muscle of the left ventricle at the site of rupture was 1.5 centimetres thick. The valves were normal. The coronary arteries did not show any abnormality, and no thrombi were found. Except for a small patch of calcification in the ascending portion, the aorta was normal. There was no fatty infiltration of the heart or aneurysmal dilatation. The heart with the pericardium weighed 14 ounces.

There were no injuries to other organs. The previous history of the patient could not be obtained. The stomach showed marked thinning of the musculature and atrophic gastritis.

Case 2.—A., male, gold miner, 45 years of age. History of attacks of pain in the chest for the last five years. Two days before death, he had a severe attack of pain, and attended a hospital, where he was found to be suffering from cough and fever, with a few rhonchi in the lungs. Heart was found to be normal, no dyspnoea nor oedema. Blood showed no malaria parasites and a provisional diagnosis of influenza was made. The next day the fever continued, and he died suddenly towards the evening; the post-mortem examination was done next morning, about 18 hours after death.

Post-mortem findings.—The pericardium was thickened, and the sac contained blood-clot weighing three ounces, and about two ounces of fluid blood. The clot had formed a mould on the external surface of the heart; moreover in the left ventricle, 2.5 centimetres upwards and backwards from the apex, were two tears 1 centimetre from each other (figure 2). The upper one was S-shaped and 1½ centimetres long and the lower one was crescentic and 1 centimetre long. The parietal pericardium was thickened and the inner

surface leathery. The heart measured 9 by 8.2 centimetres, and weighed 24 ounces. The wall of the left ventricle was thick and at the site of rupture it was a little over 2 centimetres. The musculi papillaris and chordae tendinae were prominent. The valves were normal.

The aorta was empty, and extensive atheromatous plaques were present with rugosity of the intimal layer. The openings of the coronary arteries were surrounded by atheromatous plaques, and for a distance of 2 centimetres there were irregular patches of atheroma. There was no occlusion of the coronary arteries and no evidence of infarction. Other organs did not show any marked changes.

Outstanding features.—(a) The pouch-like diverticulum of the pericardium, obviously due to traction by contracting adhesions between pleura and diaphragm in case 1. (b) Absence of any obstruction to the coronary circulation in case 1. (c) The difficulty of assessing the prognosis in case 2. (d) Multiple ruptures in case 2.

Our thanks are due to Dr. S. V. Govinda Setty for the help in conducting the post-mortem examinations.

PYREXIA DUE TO BEETLE INFECTION

By B. CHATTERJEE, M.B., D.T.M., L.M. (Dub.)

Medical Officer, The Chargoja Valley Medical Association, Dullabcherra, Sylhet

A BEETLE was recovered from the stools of a patient of mine, a child of about 1½ years, who was suffering from continued fever for two weeks. On investigation the case was proved to be one of *Bacillus coli* infection of the urinary tract. This beetle was the third of its kind to have been noted to be passed with his stools within a few days. The first two flew away practically immediately after they were passed, but this one was somewhat tardy in recovering from the shock of first seeing the light and could be captured.

This boy was treated with M.&B. 693 tablets for his urinary infection. His temperature became normal at the end of third week but remained normal only for three days and then again rose to about 102°F. and it is for a week keeping up at this level with slight intermission. He is now being treated with Mandelic, but with not much effect on his temperature. His urine has improved; only a few pus cells were seen but no *B. coli*. Blood was examined but no malaria parasites were detected.

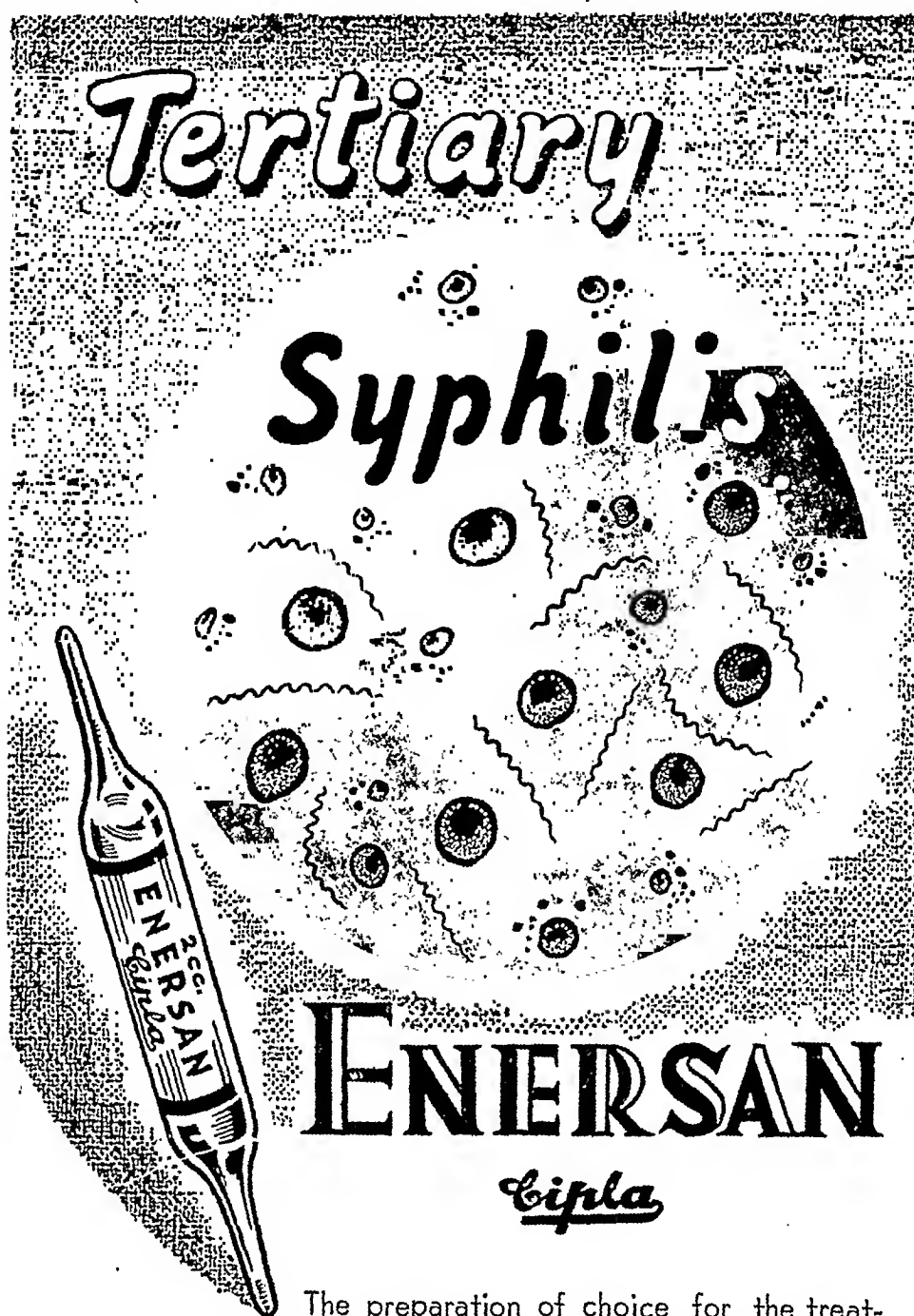
Can this continued temperature be due to the presence of this *Sarcophaga* (?)* beetle in his intestines?

*The beetle sent by Dr. Chatterjee was kindly identified by Professor D. N. Roy, who reports as follows :—

Identification : Order	.. Coleoptera.
Family	.. Scarabaeidae.
Sub-family	.. Scarabaeinae.
Genus	.. <i>Caecobius</i> .

The specimen belongs to the class of insects commonly known as dung beetles which are generally coprophagous in habit and breed in dung of all kinds. The medical interest attaching to these beetles lies in the fact that they are often voided with the stool by children and this condition is generally associated with certain symptoms such as indigestion, diarrhoea, dysentery, low fever, and emaciation. From time to time the insects are passed always in a living state mixed up with the stool. They soon clear themselves of the faecal matter and fly away.

This condition of scarabiasis has been dealt with by Strickland and Roy in the *Indian Med. Gaz.*, 1939, 74, 247.



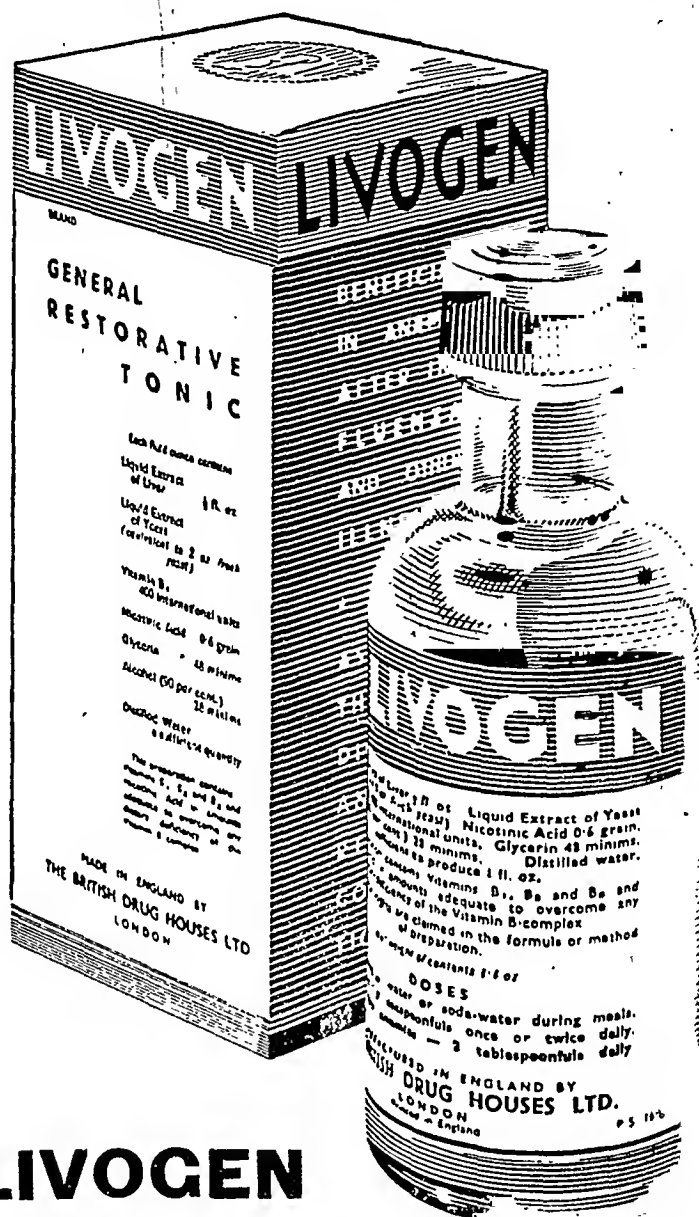
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Indian Medical Gazette

FEBRUARY

AMŒBIC DYSENTERY AS A WATER-BORNE DISEASE

AMŒBIC dysentery is always looked upon as an essentially sporadic disease. The present-day attitude towards the disease can be best shown by a quotation from the most recent and authoritative monograph on dysenteric conditions (*The Dysenteric Disorders*. By P. Manson-Bahr).

'In contradistinction to bacillary dysentery, amœbiasis shows a somewhat localized distribution; it is therefore unlikely that amœbic dysentery, liver abscess, or other complications of this infection will commonly occur in epidemic form. It can be concluded, generally speaking, that epidemics of dysentery are of the bacillary variety, while sporadic cases are due to the endemic form, which is usually amœbiasis. The so-called "epidemics" of amœbic dysentery which have been reported, especially during the last war, must, therefore, be regarded with suspicion, for they clearly indicate that there has been confusion between amœbic and other forms of dysentery; this has actually been demonstrated on many occasions'.

From the subsequent discussion on the subject, it is obvious, however, that this author looks upon water as a not uncommon source of infection, but here as elsewhere the emphasis is always on the 'carrier' and on the dissemination from this source through 'fingers, flies, and filth', that is, by direct contamination of food by food-handlers and flies, and by means of uncooked vegetables and salads in the growing of which human sewage is used as manure.

It is of course obvious that the case-to-case passage of infection that occurs frequently in bacillary dysentery will be rare in the amœbic infection, because the main forms that the patient excretes in the acute stages are not viable and infective, as are the dysentery bacilli, which are excreted in their largest numbers during an acute attack. On the other hand, it is during convalescence, when the patient ceases to be under medical control, that he passes the infective forms and is most dangerous. This fact is of course always emphasized, but the recent tendency has been to think of the dissemination of the infection only by food-handlers and to forget the possibility of such persons infecting water supplies. The danger is all the greater because ordinary methods of disinfection, such as chlorination or the addition of permanganate, do not kill the infective forms, the cysts of *Entamœba histolytica*.

The notorious Chicago hotel epidemic, not only provided a good example of water-borne epidemic of amœbic dysentery, but it showed

how the attitude of the public health authorities, which was at first the orthodox one, changed as the epidemic developed. The first step that they took was the examination of all food-handlers; amongst these they found a large percentage of cyst-passers. This source of infection was eliminated, but fresh cases occurred; a re-examination of the staff showed that many who were previously free from cysts were now passing them; the whole problem had to be reconsidered and, eventually, serious sanitary defects in the hotels were brought to light, including cross-connections between the drainage and the fresh water systems. The first water-borne epidemic in Chicago was followed a year later by another water-borne epidemic, in the same city, but in circumstances which were quite different. On the latter occasion, during the great stockyard fire of May 1934, an unfiltered water supply was used for drinking by a large number of persons, mostly firemen and spectators; amongst the bowel infections that resulted from this incident, there were a large number of cases of amœbic dysentery.

This second incident emphasized the importance of water as a medium for the transmission of amœbic dysentery. It was an isolated incident, due to very special circumstances that are unlikely to recur, but it drew attention to the dangers of an unfiltered water supply; the stockyard workers knew that there were two water supplies, one of which was not safe for drinking, but the visitors did not and the public tends to think that everything that comes out of a tap is safe for drinking.

In 1914, emetine, a newly discovered drug that had worked wonders in dysentery in India and elsewhere, had brought amœbic dysentery into the limelight; further, the textbooks all stressed the fact that amœbic was the dysentery of the tropics while bacillary had a more universal distribution. It was therefore not surprising that at Gallipoli and in Iraq, at any rate for some time, all dysenteries were thought to be amœbic and usually treated as such.

It was later found that in many war theatres, about 90 per cent of the dysenteries were really bacillary, and for the last twenty years the textbooks and army training manuals have been rubbing in this fact. The army medical officer is therefore taught that the great enemy is the dysentery bacillus, and that his preventive measures must be aimed against this organism. Fortunately, most preventive measures aimed at the bacillus will also hit the amœba, but not all, and as we have already said the chemical treatment of water supplies that will destroy the typhoid or the dysentery bacillus does not touch the cysts of *Entamœba histolytica*.

The present indications are that, in the majority of cases, the dysentery amongst the troops, at any rate the British troops, in India to-day is amœbic. We wonder whether the possibility that much of this amœbic infection is acquired from water is being borne in mind.

Special Articles

A DESIGN FOR A PLANT FOR DRYING BLOOD PLASMA OR SERUM

By BRIAN R. DYER

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and

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I. Introduction

THE drying of serum or plasma from the frozen state has been amply demonstrated to produce a transfusion material free from limitations of temperature during storage and transport, and capable of being reconstituted with pyrogen-free water at any time for use, without impairment of physiological or pharmacological properties.

The various methods of desiccation of serum and plasma have been reviewed by Strumia *et al.* (1941). Standard equipment employing some of these methods is marketed by American and English firms. However, difficulties experienced in importing any of these under present shipping conditions gave us an opportunity to design and build from local material a plant embodying several improvements and suited to conditions prevailing in India. This was made possible through a grant generously provided by the Indian Research Fund Association. The details of the design and working of this plant are presented in this paper.

II. Basic principles

Plasma or serum is frozen in the form of a shell inside glass bottles at -20°C . and placed in a chamber, the pressure in which is subsequently reduced below that of the vapour tension of plasma or serum at the temperature. The water vapour given off under these conditions from the frozen material is adsorbed by dry silica gel kept in another chamber in communication with it. As the adsorbing capacity of silica gel in that chamber becomes reduced, it is cut off, and a second chamber containing fresh gel with a vigorous adsorption capacity is put into communication with the plasma or serum chamber. Meanwhile the gel saturated with vapour is taken out and reactivated by heat. This cycle can be repeated as often as necessary. During the process of sublimation in high vacuum, the latent heat of evaporation tends to lower the temperature of frozen plasma or serum below -20°C ., thus reducing the rate of sublimation. To counteract this, heat is provided by hot water pumped through coils.

The adsorption of moisture by the silica gel results in production of heat which retards the rate of adsorption. Provision is therefore made to take away this heat and maintain the gel at a temperature low enough for efficient adsorption,

by means of cold water pumped through similar coils.

Thermoeouples imbedded in appropriate places indicate the temperature of plasma or serum during desiccation and of the silica gel during adsorption. Thermometers in the inlet and outlet of the two circulating coils indicate the heat exchange.

By appropriate regulation of heat input the temperature of the frozen plasma or serum is maintained at -20°C . When most of the moisture is given off, the heat input tends to increase the temperature of the desiccated material without increase in pressure, thus indicating that the end point of desiccation is approaching. The temperature of the dried material is then allowed to rise to 37°C . and maintained at that state in a high degree of vacuum to reduce the residual moisture to below 1 per cent.

A simple form of vacuum gauge indicates the pressure in the system.

III. Description of the plant

The plant is designed for processing 6 litres of plasma or serum disposed in 250 c.cm. lots in 500 c.cm. narrow-mouthed bottles specially designed for the purpose.

The plant consists of (1) Prefreezing unit, (2) Desiccating equipment, (3) Silica gel regenerating equipment.

Prefreezing unit (figure I)

This consists of a rectangular sheet-iron tank partitioned into three chambers and insulated with cork. Two of these chambers contain brine, and the third serves as a cold storage space for keeping frozen bottles. Each of the three compartments has an expansion coil independently connected to an ammonia compressor, and thus the temperature in any chamber can be maintained as desired. The concentration of calcium chloride brine is adjusted to give -30°C . The larger of the two brine compartments contains a system of parallel roller shafts driven by gearing, on which 24 bottles containing serum or plasma can be laid and kept rotating at the rate of about 2.8 r.p.m., while immersed in brine to a depth of $\frac{1}{2}$ inch. The brine is maintained at a uniform temperature by a screw stirrer at the bottom of the compartment. The bottles are made of special resistant glass capable of standing low temperatures. The walls of the bottles are of a uniform thickness of 3 mm.—to avoid unevenness in the frozen shell. The bottles are capped with a vaccine sleeve-type rubber stopper before being laid on the rollers.

Desiccating equipment (figure II)

The plasma or serum and silica gel chambers are identical and interchangeable. They are made out of $\frac{3}{8}$ -inch thick mild steel welded into a cylinder 16-inch diameter and $25\frac{1}{2}$ -inch high including the bottom. The lid is made of $\frac{1}{2}$ -inch thick steel in which a tapered groove is machined accurately to fit a corresponding tapered tongue

on the top of the cylinder, so as to get a vacuum tight fit. The lid is provided with a lifting handle. A 2-inch diameter steam quality standard long bend welded to the bottom of the cylinder connects on to a flanged tee piece through a rubber gasket, and thence to the other two cylinders through two vacuum taps of gun metal. This 2-inch pipe is the duct through which moisture travels from the plasma or serum chamber to the silica gel chambers.

The bottles are placed on a galvanized iron basket with three annular trays.

There are two sets of helical copper coils of $\frac{3}{8}$ -inch diameter, one inside the other, in each cylinder. In the interspace between the two coils, the baskets containing plasma or serum bottles or silica gel make a fit with a clearance of $\frac{1}{4}$ inch. For rigidity and for the better transference of heat, the inner and outer coils are soldered on to a cylindrical copper sheet 1/16-inch thick. The inlet and outlet to the coils are both taken through the bottom of the cylinder with a special adaptor to take up unequal expansion without detriment to the vacuum.

Besides the main duct of 2-inch diameter there is a copper pipe of $\frac{3}{8}$ -inch diameter taking off from under the basket in each chamber, and leading through a vacuum tap to a common cross pipe connected to the vacuum pump. Thus, any of the chambers can be evacuated independently of the others as required.

The two large 2-inch vacuum taps are made of gun metal. They depend on a perfectly machined taper fit of about 5° , a zig-zag outlet, and an oil seal at the top. The $\frac{3}{8}$ -inch vacuum taps are also similar in design.

Two nipples are provided on the lids of the two silica gel chambers to destroy the vacuum.

Three small tubes welded to the sides of the three chambers near their top provide outlets for thermocouples.

The thermocouples are of copper and constantan wires, 22-inch gauge, passing through the walls of the chambers through low vapour tension waxes such as Everett's or a mixture of resin and beeswax melted together and kept in high vacuum.

The inlet and outlet pipes of the water circulation systems of all three chambers are so designed as to enable either hot or cold water to be circulated into any one or more chambers as desired. The valves controlling these systems are all grouped together on the table, and thermometers have been mounted on tee pieces in these pipes so that the temperatures of the water at the inlet and outlet can be read off. Preliminary calculations disclosed that only pumps of small capacity (not more than 15 gallons per hour) would be needed. A diaphragm pump used for pumping petrol in motor cars was found to be the most suitable, flexible, cheap and readily available for the purpose. A fractional-horse-power electric motor with a crankgear actuates the rocker of this

pump. The pump can be set to work at any desired rate by altering the stroke of the rocker. This kind of pump has been found entirely satisfactory in use, and pumps away for days even when buried completely under 2 inches of snow. This pump can be readily dismantled and cleaned, and spare diaphragms are also available. Two pumps are in use, and either or both can be used for pumping hot water or cold brine.

The hot water is provided by a small gas-burning domestic hot water heater of the 'Ascot' type. It is stored in a cork-lined sump of about 4-gallon capacity. Cold brine is taken off from the small compartment in the prefreezing tank already mentioned, and returned to the same tank after circulation.

The vacuum pump is a Geryk rotary single-stage Duplex pump capable of a displacement of 2.4 cubic feet per minute and an ultimate vacuum of .00001 mm. mercury off perfect. A specially designed screen at the inlet of the pump prevents suction of gross and gritty foreign matter into the pump mechanism. The vacuum gauge used is a 'Vacustat' made by Edwards, with a range from 10 mm. to .01 mm. It is connected to the system by pressure tubing. It is normally kept in a horizontal position, and is tilted vertically only at the time of taking a reading. The pressure is read directly on the scale. After reading, the gauge is returned to the horizontal position. The vacuum is read at a point midway between the plasma or serum and the silica gel chambers. The silica gel used is granular and is retained on Tyler's standard screen No. 20 (size of opening 0.833 mm.). About 40 pounds of silica gel are distributed in each chamber in 23 annular aluminium trays in layers about $\frac{3}{4}$ -inch deep. These trays are perforated at the bottom, and form a basket which is lowered into the chamber between the inner and outer cooling coils, by means of a portable hoist.

As the transference of heat by radiation alone from the cooling coils to the plasma or serum and silica gel is likely to be unsatisfactory, even when the intervening space is $\frac{1}{4}$ inch, and there will be no convection in vacuum, copper brushes are used to conduct heat by direct metallic contact between the trays and the copper drums to which coils are soldered. These brushes consist of about 24 copper pieces of $\frac{1}{2}$ -inch square section, so fixed that they will not interfere with the easy introduction or removal of the baskets. Further, the bottles of plasma or serum are placed in slit copper tumblers during desiccation.

Thermocouples are led off as described earlier. The E.M.F. developed in the thermocouples is measured in a potentiometric system reading correct to 10 microvolts or approximately $\frac{1}{4}^\circ\text{C}$. The reference junction is at ordinary room temperature. In order to get the correct temperature, a chart prepared from the standard Adam's table is used after adding the potential

due to room temperature algebraically to the observed potential.

Silica gel regenerating equipment (figure III)

The silica gel is regenerated in a special electrical drying oven, which is only a welded steel cylinder, provided with a lid having a taper flange carefully machined. The heater elements are disposed at the bottom, middle and top of the cylinder, to obtain uniform heating of the entire mass of silica gel. There is a $\frac{1}{2}$ -inch pipe outlet for moisture with a tap at the top of the lid. This outlet can be connected to a reciprocating pump which can produce a vacuum of the order of 25 inches in the oven. The oven is also provided with a vacuum gauge and an opening for a mercury thermometer on

with our experience. If, at the end of 5 hours, the outlet for moisture is connected to the reciprocating pump and pumped, considerable quantities of steam can be seen coming out of the oven for the next 5 hours, showing that the silica gel could not possibly have been dry in 5 hours. Indeed, we consider that it is essential to keep on pumping the contents of the silica gel oven until no more steam is noticed. A more delicate test is to observe whether a cold glass is not fogged. When this stage is reached, the suction pump is worked for some more time until the vacuum gauge reads 25 inches. When this reading is obtained, the tap on the outlet pipe is closed, the pump stopped, the heater switched off and the silica gel allowed to cool in the vacuum. This takes about 5 hours. Then the

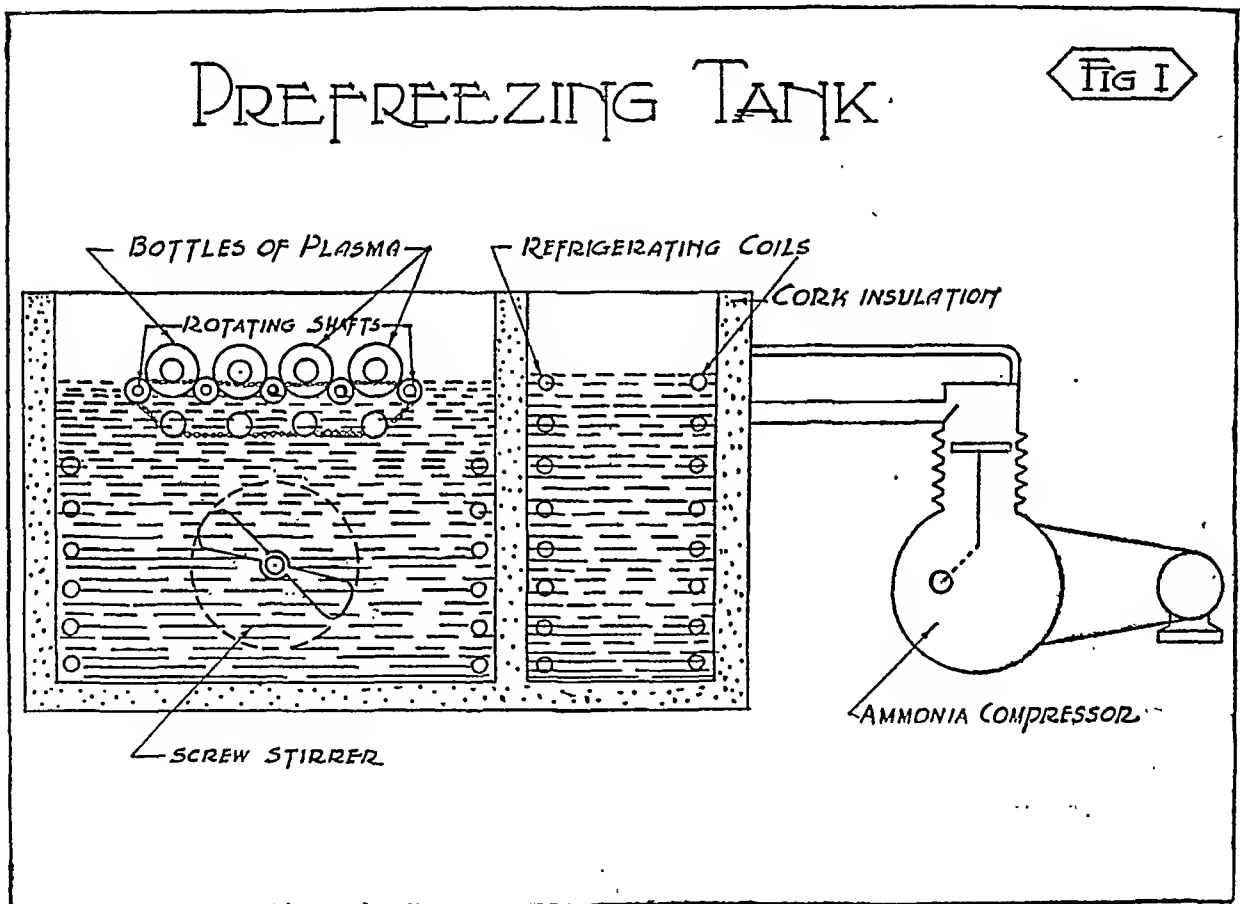


Fig. 1.

the side wall. The total wattage of the oven is 5,200 watts distributed in 12 elements.

IV. Working of the machine

The first thing to do is to dry the silica gel. This is accomplished by putting it into the oven, putting on the lid and switching on the 3 heating elements. In about an hour, the temperature inside the chamber will reach 150°C . After this, by switching on and off some groups of elements, the temperature is maintained at 150°C . It is usually said that 5 hours of heating at 150°C is sufficient to dry silica gel. This is not in accord

oven is opened, and the basket is lifted up by the hoist, and weighed quickly with as little exposure to the atmosphere as possible.

After weighing to the nearest ounce, the basket is put into the silica gel chamber quickly and carefully after checking whether the brushes are in place. The thermocouples are then embedded in the gel. Meantime the lid is prepared as follows: The groove is warmed up by means of a gas jet and filled with low vapour-tension Apiezon Q wax. It is then placed in position over the chamber on the left (figure 2). With the 2-inch vacuum tap VT_c closed and the

small tap VT₂ only open (all others being closed), the vacuum pump is switched on and the chamber is exhausted. If the lid is in proper position, the Apiezon wax is expelled as the lid gets set in its seating. The vacuum assists in seating the lid. A perfect vacuum joint is obtained by pressing in the exuded wax all round the groove. After working the pump for about 10 minutes VT₂ is closed. In a similar manner the other silica gel chamber is also charged with dry silica gel. With these two charges the machine is ready for the desiccation process.

Prefreezing

The bottles are capped with sterilized sleeve-type serum stoppers of India rubber and then

as to pass under the sleeved stopper. This thermocouple is sterilized in a Petri dish before introduction into the sterile bottle. After filling with 250 c.cm. of serum or plasma, the bottles are laid over the rollers of the prefreezing tank when the brine has attained a temperature of -30°C . The rollers are kept rotating, and the whole mass of plasma or serum freezes as a shell about 1 cm. thick in 15 minutes. The bottles are then taken out one by one, and under careful aseptic precautions the sleeve stoppers are removed and replaced by sterilized caps, each consisting of two layers of butter muslin sandwiching a layer of loose cotton-wool $\frac{1}{8}$ -inch thick. The cap is tied in position by a noose around the glass mouth. Covering the whole

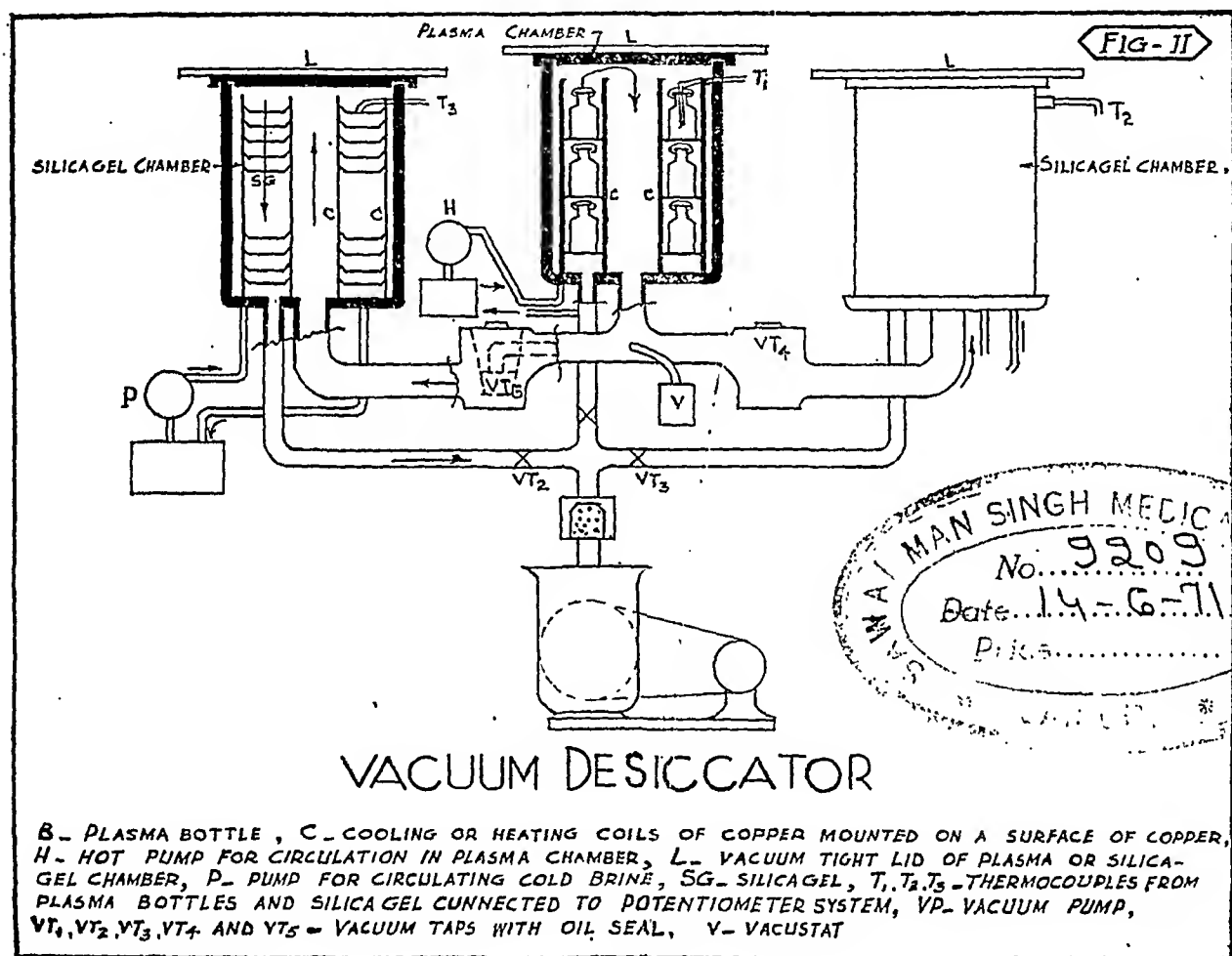


Fig. 2.

filled with serum or plasma by closed aseptic technique. 250 c.cm. of serum or plasma are placed in each bottle. One of these bottles contains a sterilized thermocouple junction stretching down to the bottom. The thermocouple is prepared as follows: Half an inch of the enamel on a 6-inch length of copper wire 22-inch gauge and a half inch of the oxidized surface of constantan wire are scraped with a sharp safety razor blade and twisted together by clean pliers. The couple is then bent to suit the shape of the bottle and bent double near the mouth, so

of the gauze cap is placed a sterile cellophane membrane kept in place by an elastic rubber band. Each bottle is then put back on the rollers for further hardening of the frozen shell.

Meanwhile, the plasma or serum bottle basket is kept in a cold room. Cold brine is circulated in the plasma or serum chamber. After about half an hour the plasma or serum in the bottle would have attained at least -20°C ., and the plasma or serum chamber at least -10°C . The bottles are expeditiously taken out one by one and immersed in rectified spirits (previously cooled to -25°C .)

to wash out calcium chloride. The rubber bands and the cellophane covers are then removed and the bottles are pushed into slit copper tumblers and loaded on the trays. The basket is quickly lowered into position in the plasma or serum chamber. The thermocouple bottle is kept on the top and the thermocouple wires are connected to two heavier gauge wires of the same two metals, led through the wall of the chamber and then joined on to copper leads by means of a double porcelain cleat. The lid of the chamber is then put on quickly as was done in the silica gel chamber.

The vacuum pump is started, and the chamber is evacuated keeping VT_5 and VT_2 open and taps VT_4 , VT_1 and VT_3 closed. As soon as tap VT_5 is opened, the vacuum in the silica gel chamber brings down the pressure in the plasma or serum chamber quickly, thus making conditions favourable for the commencement of sublimation. The entire system can be evacuated in the course of 20 minutes to 500 microns. In another 10 minutes the pressure will drop to 400 microns, when sublimation is bound to be rapid as it is very much below the vapour tension of ice at -20°C . (770 microns). There is no danger of thawing of the plasma, as cold brine is circulating in the plasma chamber as well as the silica gel chamber. The circulation of cold brine in the plasma chamber in the earlier stages is a great advantage in a tropical climate where the danger of thawing is much greater than in a temperate climate. This is particularly valuable if there is any leakage or breakdown preventing the attainment of the requisite vacuum in less 30 minutes.

The temperature of the plasma or serum is recorded on and before attaining the vacuum of 400 microns and it should be around -20°C . With rapid evaporation under this vacuum, the temperature may drop below -20°C . and in the course of one or two hours it may touch -30°C . Then the cold brine circulation in the plasma chamber is stopped. After this the temperature of the plasma or serum rises steadily to -20°C ., without any circulation. The system absorbs heat from the atmosphere to supply the latent heat of evaporation most of the time through the efficient heat transference by conduction.

From now on, pressures are recorded every half hour and the temperatures are recorded every one hour. The pressure should be maintained below 770 microns and the temperature about -20°C . The vacuum pump cannot be stopped at this stage because it performs the essential function of drawing the sluggish molecules of water vapour through the silica gel. The function of the pump is that of an exhaust fan for circulation of vapour. If at any time the plasma or serum temperature rises above -20°C . cold brine circulation can be resumed and will have the effect of reducing the temperature of plasma or serum and controlling the rate of sublimation. In due course the adsorption capacity of silica gel will be progressively reduced, while the frozen plasma or serum will

go on producing vapour in the vacuum. Under these conditions the pressure will rise, and the plasma or serum temperature will also rise. If the pressure persists above 770 microns and the plasma or serum temperature rises above -20°C ., it will be necessary to switch on the next charge of silica gel by closing VT_5 and VT_2 and by opening valves VT_4 and VT_3 . We consider from experience that the silica gel should be changed every 12 hours for the best results. As soon as the fresh silica gel is put in communication with plasma, there is a quick fall of pressure and temperature, due to rapid adsorption of moisture and rapid evaporation. As soon as one

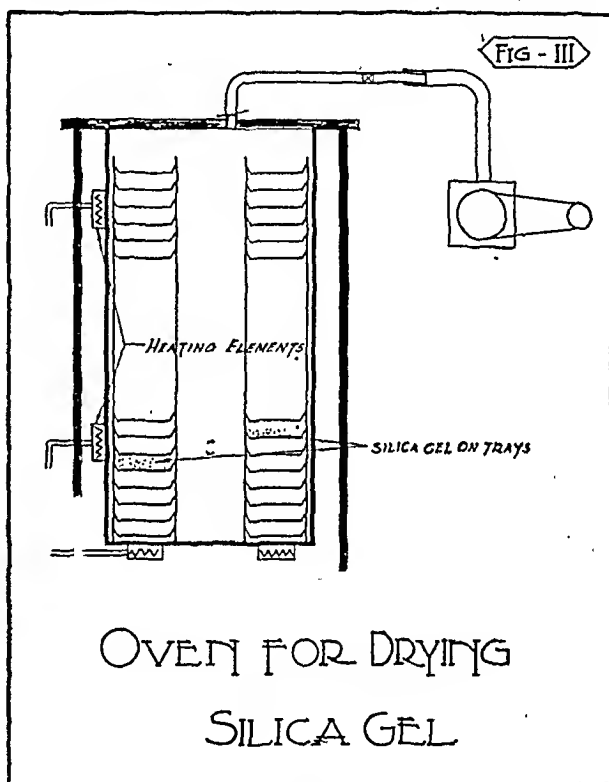


Fig. 3.

charge of silica gel becomes inactive, that chamber is disconnected. The inactive silica gel is removed and weighed to find the weight of moisture adsorbed from the plasma or serum. The inactive silica gel is put into the oven and regenerated in the usual manner. A fresh charge of dry regenerated silica gel must always be on hand to replace the inactive charge taken out. It must be kept in vacuum, ready for use.

In due course, the vacuum will improve to 200 microns, and the temperature of the serum or plasma will tend to rise above -20°C . This is an indication of the approach of the ending stage of desiccation.

If during the run there is any mechanical or electrical breakdown, and the temperature of the plasma or serum tends to rise, and the pressure also rises, it is possible to control the situation by immediately circulating cold brine in the plasma or serum chamber and keeping it well frozen. This is a feature not found in any of the other plants so far designed.

As the end point of desiccation approaches, the plasma or serum temperature steadily rises above 0°C . with steady improvement of the vacuum. This happened in about 50 hours with a single charge of silica gel. A graphical record of the temperature and pressure during a complete run is given in figure 4. The time may be appreciably shortened if the number of fresh charges of gel is increased during the period. At this stage, water at room temperature can be safely circulated in the plasma chamber till the plasma or serum temperature becomes equal to that of the circulating water. Now the vacuum pump can be safely stopped for even as long as an hour. If it works for 5 minutes it can restore the vacuum to the original level. After this, hot water at 40° to 45°C . may be circulated till the plasma or serum temperature rises to 37°C .

on this rubber stopper and the bottle is packed and sealed in a tin container.

The dried serum is very pale yellow in colour, still retaining the shape of the frozen mass. On shaking it crumbles into a fine powder of crystalline appearance.

The moisture content of specimens obtained by this process was less than 1 per cent. The dried serum dissolves easily in pyrogen-free distilled water and can be reconstituted in less than 2 minutes.

Summary and conclusions

1. Serum and plasma dried from the frozen state have been proved to be good substitutes for blood, fresh serum or plasma in transfusion, and machines have been designed for carrying on the process of drying.

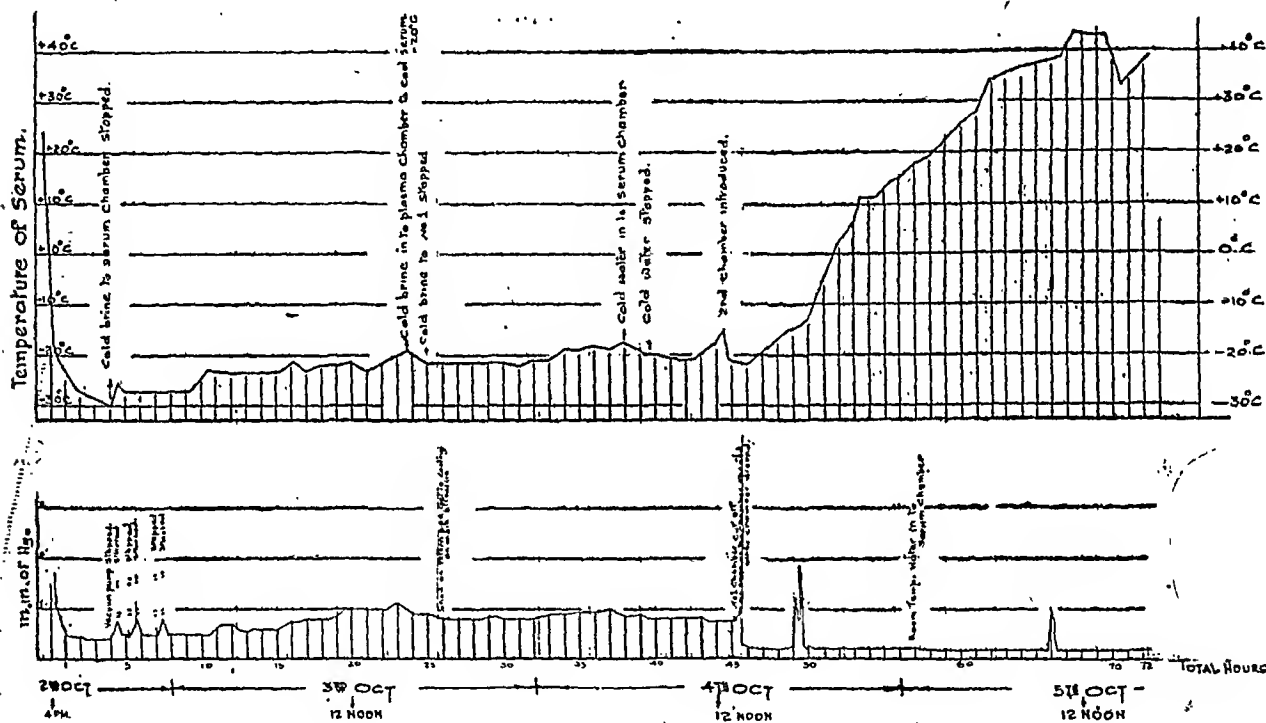


Fig. 4.

Desiccation is continued with plasma or serum at 37°C . by regulation of hot water circulation for 10 to 12 hours more. At the end of the process the vacuum pump is stopped, and air is let in through the silica gel chamber, which helps in keeping it dry.

When the chambers are at atmospheric pressure, the lid of the plasma or serum chamber is easily taken off. The plasma or serum basket is taken out, the bottles are taken out of the copper tumblers, the gauze caps are removed and replaced by sterile sleeve-type vaccine rubber stoppers. The stoppers are pierced with a hypodermic needle and a vacuum of the order of 29 inches is produced by a Hyvac pump. The needle is then quickly taken out and the puncture point as well as the edges of the stopper are painted over with sterile beeswax-resin mixture. Finally a viscose cap is slipped

2. As it was difficult to import such a machine under existing war conditions, the Indian Research Fund Association generously provided a grant for building a plant specially designed at the All-India Institute of Hygiene and Public Health, Calcutta.

3. The basic principles of this design are briefly stated.

These include sublimation of ice from the plasma or serum in the frozen state at -20°C . at the appropriate vacuum, and adsorption of the vapour by silica gel which can be regenerated by heat.

4. The design includes (a) A self-contained prefreezing unit using calcium chloride brine cooled from an ammonia compressor.

(b) A vacuum desiccator, consisting of three intercommunicating vacuum chambers, with

(Concluded on next page)

APPENDICITIS

THE INFLUENCE OF PATHOLOGY ON SYMPTOMS AND TREATMENT

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WITH SOME OBSERVATIONS ON X-RAY DIAGNOSIS

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My excuse for writing on this hackneyed subject is a case I saw recently, and my reason is that in India the diagnosis of appendicitis has not reached the degree of accuracy found in countries where people live on a 'civilized' diet—and get appendicitis more frequently.

A few nights ago, I was called urgently to see a child. She had been under medical treatment for two and a half days, and as the parents were afraid of operation she had had sulphanilamide and 'Ochsner-Sherren' treatment. I found her showing much toxæmia with a running pulse of 160, a temperature of 102.2, and an acutely tender lump in the right iliac fossa, with general abdominal tenderness. I diagnosed an appendix about to burst and operated within the hour. I found an acutely inflamed appendix which had ruptured into a thin sac of omentum and was about to spread infection all over the peritoneum. I removed the appendix and drained the site and the child recovered, but how much easier and safer the operation would have been two and a half days earlier.

(Continued from previous page)

vacuum taps, in one of which plasma or serum is kept and the other two chambers can be charged alternately with active silica gel during the process of desiccation. Temperatures in these chambers are controlled by circulation of hot or cold water and read by thermocouples. Vacuum is measured by a suitable vacuum gauge.

(c) An electrically heated oven for activating the inactive silica gel in vacuum with a pump.

5. The working of the plant consists of pre-freezing the serum or plasma, regeneration and charging of silica gel, and producing a high vacuum in the desiccator while maintaining thermal control over the frozen plasma or serum and the gel. The end point of desiccation is attained by the maintenance of a vacuum of the order of 200 microns or less for about 12 hours while the temperature of the dry product is raised and kept at 37°C. This produces a dry powder with moisture content of less than 1 per cent and high solubility. The process takes about 72 hours and can be shortened further with more frequent changes of silica gel.

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In the clinical part of my examination for the M.R.C.P. one of the Censors asked me 'What would this lady's lungs look like in a bottle'? I do not know what the lady thought, but I have often thought what a wise question that was, for it is only by visualizing the organs we are treating that we can give rational treatment, and it is with this idea in mind that the present article is written.

Ætiology

Though this is generally considered obscure, there are certain facts which have a very direct bearing.

Diet.—This is the important factor. In Willkie's famous experiments with isolated loops of cat's ileum, the loops full of protein became gangrenous, in a few hours, those with carbohydrate developed an abscess or mucocoele, and the empty loops became mucocoeles.

Many others besides myself have observed the relative rarity of appendicitis among rural vegetarians in India and its frequency among city-dwellers eating a mixed diet, but the most striking evidence I have met was my own experience in Burma when I was surgical specialist there twenty years ago. I was in surgical charge of many more Burmese than British troops, but although in the course of my five years there I removed many an inflamed British appendix, I did not remove a single Burmese one. Main items in the Burmese diet were rice, atta and dāl, and in the British, meat, potatoes and bread. The latter forms of starch are more glutinous than the former and probably predispose to intestinal and appendicular constipation. The prophylaxis of appendicitis is therefore suggested, but I think that most Europeans would rather risk appendicitis than change their diet.

Over-eating.—As already remarked, appendicitis is far more common in the sedentary town-dweller, who does not need most of the rich food he eats, than in the countryman, who puts his more bulky diet to real use. Even if due allowance is made for shortage of civilian surgeons and hospital facilities, I think that after the present war it will be found there has been a decrease in appendicitis in the starved areas.

Constipation.—This depends largely on diet, exercise and sex, while its sequel, the habitual taking of purgatives, by inducing a chronic catarrh of the lower bowel, is probably an ancillary factor. The fact that a concretion so often causes ulceration and perforation of the appendix brings home the importance of constipation, that bane of civilization and blessing of the patent-medicine vendor. If, however, it were of prime importance, appendicitis would be far commoner in women than in men, because the constipation ratio must be about ten women to one man, while the appendicitis ratio is about three men to two women. We therefore conclude that constipation aggravates the condition but does not cause it. Liquid paraffin with a

high-carbohydrate-low-protein diet is a useful prophylactic for cases awaiting interval appendectomy.

Heredity.—The disease often seems to run in families, though this may be due to dietetic or other factors, perhaps even to the diagnostic inclinations of the medical attendant, but so far no constant familial predisposing anomaly has been discovered, except perhaps the retro-cæcal appendix.

Other diseases.—For some reason, children who suffer from tonsils and adenoids seem very liable, even years later, to appendicitis, possibly because the unhealthy state of these organs is shared by the appendix, which contains a large amount of lymphoid tissue. Typhoid fever, tuberculosis and dysentery are occasional ætiological factors, while thread-worms, round-worms or foreign bodies may be found in the appendix.

Previous attacks.—As pointed out later, a fibrotic, stenosed appendix is obviously handicapped in a fight against opposing organisms and is likely to retain a concretion; it should therefore be removed.

Some anatomical points

Roughly, the appendix may be in one of three positions, in order of frequency :—

(a) 'Normal' (about 50 per cent). The organ has a mesentery and lies free in the peritoneal cavity with the tip pointing towards the spleen.

(b) Retro-cæcal (about 40 per cent). The meso-appendix is very short or absent, the appendix being as a rule directly behind the cæcum, though it may lie on either side of it. The tip points upwards and the organ may be very long.

(c) Pelvic (about 10 per cent). The appendix dips over the brim of the pelvis or lies in it.

At operation the retro-cæcal appendix is commoner than in the dissecting room, possibly because its situation may predispose it to disease. A little reflection will show that each of these positions offers differences in symptoms, signs, spread of infection and site of abscess. An experienced surgeon can often forecast the position and state of the appendix, but even the elect may be deceived, which gives zest to the problem and encouragement to others.

Pathology, with notes on accompanying symptoms

This will be considered under the following heads :—

Catarrh.

Acute inflammation.

Gangrene.

Recurrent appendicitis.

Chronic appendicitis.

Effects of position of appendix.

Catarrh.—We can dismiss this in a few words, as genuine catarrh is part of a widespread

intestinal condition following the ingestion of contaminated food and accompanied by diarrhoea. Its description as a separate entity is based more on analogy with other mucous membranes than on pathological findings. As the owner is unaware of his appendix unless it is in a state of spasm or its peritoneal coat is stretched or inflamed, catarrh in itself is symptomless.

Acute inflammation.—Just as boils begin in the hair follicles or in the sweat glands, so appendicitis probably begins in Lieberkuhn's follicles or in the solitary glands, with both of which the appendix is richly supplied. From here the inflammation spreads rapidly in the submucous layer, causing pressure on the lymphatics and small veins. The appendix begins to swell, and within a few hours the infection has reached the peritoneal coat.

Now, the peristalsis-stimulating nerve of the appendix, as of the rest of the gut, is the vagus, which terminates in Auerbach's plexus between the muscular layers. Inflammatory obstruction of the appendicular outlet, combined with inflammatory irritation of the plexus, therefore rouses the appendix to a fine fury of forcible contraction, which, together with the distension of the organ, causes acute pain. The physiology is not certain, but the pain impulses probably reach the brain *via* the solar plexus and the lesser splanchnic nerve, which it will be remembered connects with the ninth, tenth and eleventh dorsal segments, exactly the level at which the pain is felt.

It is important to distinguish between this early visceral pain and the localized pain which does not begin until the parietal peritoneum becomes affected. The early pain is referred vaguely to the deep mid-abdominal region, it does not vary with the position of the appendix, it comes on in spasms and is associated with nausea and vomiting; localized pressure produces generalized pain and increases the nausea, a point that helps to distinguish the condition from ordinary colic, where pressure brings relief and the patient often holds his abdomen during spasms. These early signs are not always observed, but they are seen at their best in children, and unfortunately are often thought to be caused by a bilious attack. It cannot be too strongly urged and too constantly remembered that an attack of abdominal pain with vomiting, especially in a child, should be looked on as appendicitis until proved otherwise. In my experience, even in the early stage a careful abdominal and rectal examination will generally reveal some localized tenderness, though its absence does not exclude appendicitis, while the pulse and temperature are usually raised slightly, the former more than the latter. Should one operate in the presence of these equivocal early signs? The answer is 'Yes' if there is localized tenderness: 'Yes' if the patient is under fifteen or over fifty, and 'Yes' if the symptoms are obviously severe or increasing. But the point is discussed in more detail later.

Further progress is naturally variable, depending on the ferocity of the attack and the strength of the defence, but in an average acute case the condition at the end of a further 24 hours is as follows: the appendix is intensely red, congested and swollen, about the size and shape of a bent little finger; the mucous membrane is thickened and ulcerated, the wall teems with leucocytes, the now roughened coat is covered with flakes of purulent lymph, and is lightly adherent to surrounding structures. The most serious thing, however, is the threat to the veins, thrombosis of which will cause gangrene, the veins of the meso-appendix being also thrombosed in a severe case. By now the parietal peritoneum is becoming inflamed, producing the so-called 'typical' signs of acute appendicitis, which are, of course, rigidity and tenderness in the right iliac fossa. As the patient's temperature is probably between 99 and 102 and his pulse between 90 and 130 the diagnosis of acute appendicitis is obvious and the treatment, immediate operation, equally so.

If all cases conformed to the above plan, diagnosis would be easy, but 'Nature moves in circles: Art in straight lines', and part of the fascination of our craft lies in trying to find out what Nature will do next. At the stage now reached one of several things may happen. The whole affair may settle down, but the appendix is left with some fibrosis and perhaps some adhesions, so not only is it liable to further attacks, but also it will be handicapped if they should occur. If the case is first seen in the defervescence stage, more than 48 hours after symptoms began, sulphanilamide Ochsner-Sherren treatment is correct. The patient is put in the high Fowler position and given nothing by the mouth except water and sulphanilamide, the pulse and temperature being charted every two hours. If unfavourable signs appear, such as increase of pulse, pain or tenderness, if the patient vomits or seems to be deteriorating, then immediate operation is done. Perhaps Ochsner-Sherren treatment would be less abused—in both senses of the word—if it were more realized that such operative interruption forms part of it.

Another essential part of the treatment is a competent nurse. If all goes well, during the first three days the temperature will show a distinct but diminishing evening rise, and on the fourth the patient may be given a little liquid nourishment. In India this treatment often fills the relations with a fear that the patients will starve to death; they may be reassured if they are told that most people can live for at least three weeks on water, but they are more likely surreptitiously to give the patient a meal. This is one reason for the need of a competent nurse. By the end of a week the symptoms will usually have subsided, and the appendix is removed some two months later, by which time the inflammation and plastic adhesions have disappeared.

The attack may, however, be too severe or the resistance too weak for palliative measures to be successful, or the patient may not have come under skilled treatment; in such cases the appendix becomes more and more oedematous, until the base becomes occluded. Just as in war it is a disaster to be cut off from the base, so it is in the appendix, for the natural line of retreat for the septic contents is cut and the organ becomes distended with pus. As the tension increases, a patch on the anti-mesenteric border near the tip, where the blood-supply is least, becomes completely cut off from its blood-supply and undergoes 'tension gangrene'. Through this weak spot perforation occurs, perforation at the base being commonly associated with a concretion. To revert to treatment for a moment, it is at this juncture that castor oil has caused so many deaths, because it not only makes the appendix blurt out its contents, so to speak, but by increasing peristalsis ensures that the contents are well churned up in the peritoneal cavity.

Perforation.—It is some consolation to the anxious surgeon to know that this disaster is rare during the first 36 hours of an acute inflammation, though in gangrene it can occur within 18 hours. (These figures are admittedly arbitrary, but are roughly correct.)

Classically, the signs of perforation are a sudden sharp pain followed by relief and accompanied by a varying amount of shock. The pulse rate rises suddenly and the temperature falls. After some hours the picture changes to one of generalized abdominal pain with 'board-like' rigidity, a rising pulse and temperature, absolute constipation and perhaps vomiting. Even now the cause of the peritonitis can generally be diagnosed by the position of maximum tenderness, which, taken in conjunction with the history and the other symptoms, is of the greatest help, as it indicates where the incision is to be made. It may be mentioned in passing that, apart from abdominal emergencies, this rigidity may be caused by basal pleurisy, coronary thrombosis, tetanus (quite common in India) or spinal injury. The rigidity of coronary thrombosis and pleurisy affects chiefly the upper abdomen, while that due to hysteria or malingering can be softened by distracting the patient's attention, and that due to gastric crisis is rare in India.

In some cases, as in that related at the beginning of this paper, it is possible, by carefully evaluating the history, symptoms and signs, to diagnose correctly the imminence of perforation. Sometimes a rather indefinite lump may be felt, but unlike the firm, trustworthy lump described in the next section, it is, if not composed of faeces, acutely tender, the muscle over it is rigid and the skin hyperæsthetic; a sort of crepitus may be detected, and the experienced examiner gets the impression that firm pressure would burst the appendix or its omental covering; needless to say, this must never be done. Further, gentle palpation on the opposite side

will often reveal the beginning of rigidity there and also cause pain on the affected side. All these signs point to the urgency of operation. In children below fifteen with acute appendicitis, perforation is *always* imminent unless it has already occurred.

The omentum.—In the adult this indomitable organ loses no time in getting to the seat of trouble, but it is not until after at least 48 hours or more that it is able to form a barrier strong enough to isolate it: hence the danger of the first 48 hours. When its efforts are successful it cannot only wrap up the inflamed organ safely, but can do this with such effect that an abscess and even the appendix itself can be completely absorbed. If there has been an abscess, therefore, and one contemplates doing an interval appendicectomy, it is worth while having an x-ray examination made, so as to be sure that the appendix is still there.

In a child the omentum is short, and may not reach the appendix, which is one reason for the urgency of operation; another is that the omentum and adhesions are more tender than in the adult and the inflammation is apt to be more severe.

Old people in general do not spring to action with the alacrity of the young, and this applies also to their omentum. Their pulse and temperature, like their outlook on life, are not easily disturbed, and early signs and symptoms may pass unnoticed. Thus it comes about that there may be no suspicion of appendicitis until perforation has occurred. These cases therefore require great judgment. If, when the patient is first seen, he is unlikely to live, he should be left to die in peace, but if he has peritonitis and a reasonable hope of life (in other words, if the pulse and blood pressure are good, a pulse over 120 or a systolic blood pressure below 75 being sure signs of impending dissolution in these cases), the peritoneum may be drained under a local anæsthetic and vigorous accessory treatment given. In early cases without peritonitis, it is safest to operate, while in late unperforated cases or when there is a lump, Ochsner-Sherren treatment is indicated. A fluctuating lump or a frank abscess is, of course, opened. From all this it will be seen that in old people appendicitis, though happily rare, is a serious disease, and the young surgeon or practitioner is advised to call in consultation a man of established reputation, otherwise he may lose his own.

To revert to the omentum. The clinical sign of its successful activity in a case of appendicitis is a lump, of recent origin, and varying tenderness felt in the right iliac fossa; it should be noted that it is often as low down as Poupert's ligament and sometimes as far out as the loin. The early stage of tentative adhesions, when the omentum is exploring the ground, naturally cannot be felt, the lump not usually being palpable before the third day, by which time it may contain some pus. If this is present in small amount, it is so walled off that it generally

absorbs. For this sort of case, therefore, we can state a rule. If there is a lump, wait; if not, operate. In the former case operation will do just what Nature is trying to prevent, namely, infect the peritoneum, while in the latter it will save it from infection. If, as time goes on, an abscess forms, it should be opened, but no more should be done, as attempts to remove the appendix at this stage may spread infection and prove fatal.

In those difficult cases where one is called out into the country to see a patient—perhaps a person of importance—and will have to leave him with no operating surgeon within call, it is wiser to operate unless the signs of recovery or localization are unmistakable. By this I mean that the bowels are acting normally, the pulse rate and temperature are coming down, there is no generalized abdominal tenderness, and the tongue is getting cleaner. In all cases with signs of spread, or, in these circumstances, even those that appear to be stationary, in all cases with a rising pulse rate, and in all cases of children, operation is the safest treatment. The case of the elderly patient has already been dealt with, but in the surroundings now under discussion the bias should be more towards operation if survival seems probable.

A few words may be said here about acute peritonitis and its treatment. Some members of the modern school advocate palliative treatment, arguing that a drain can deal with only a very small area of the vast peritoneal bed. The truth is that the treatment depends on the cause, and in the rare pneumococcal or gonococcal peritonitis, treatment with sulphapyridine is obviously correct. If, however, as far more frequently happens, peritonitis is due to a leaking viscus the leak must be stopped and an exit provided if much noxious fluid has already collected. If possible the appendix should be removed, a glove drain being inserted to drain the bed for two or three days. If the appendix cannot be removed it should be drained. In cases opened within a few hours of perforation the drain may well be omitted, if the appendix is safely removed. In all such cases intravenous soluseptasine is an invaluable adjuvant, and sulphanilamide may be powdered into the peritoneum and given by mouth. After operation the patient should be kept in the high Fowler position.

Gangrene.—In the limbs or any other organ the cause of gangrene is stoppage of the blood supply. It is also the cause in the appendix, and can happen in various ways, some of which have already been indicated, namely, inflammatory thrombosis of the veins of the appendix, the meso-appendix or both. In these events the symptoms of acute inflammation will have preceded those of gangrene, so they need not be further described.

Now any destructive or chronic inflammation is followed by fibrosis and cicatricial contraction, witness the stricture following urethritis or the

deformities following burns. In the same way, inflammation of the wall of the appendix is followed by stricture, and of the surrounding tissues by adhesions. It is well known that slight congestion of the urethra can cause complete retention of urine in a patient with stricture; in the same way, slight inflammation in an appendix with a stricture at the base can convert the organ into a closed sac. Swelling and tension at the stricture impair the blood-supply to the distal part, the contents rapidly decompose, and the appendix becomes distended, thrombotic and gangrenous. A similar sequence of events can be caused in a somewhat different way by the jamming of a concretion in the base of the appendix, the presence of a concretion and the act of jamming being made more likely by the presence of fibrosis.

The danger of obstructive gangrene lies in its rapidity and in the deceptive mildness of the early symptoms. A previously healthy British soldier when seen at 11 a.m. said that in the early morning he had had a sudden severe colicky pain in the abdomen, after which he had vomited and then felt slightly better; the colicky pain had continued for a few hours, but had stopped by the time I saw him. There was no significant history, his bowels had acted on the previous day and he had felt quite well until his attack. At the time of my examination the temperature was 97.8 and the pulse 88. The tongue was clean and moist and the abdomen soft and flat, but there was a very slight localized tenderness in the right iliac fossa. Rectal examination gave negative results. To my mind the combination of vomiting without diarrhoea preceded by sudden severe mid-abdominal colic, which had now disappeared, leaving behind slight localized tenderness and a slightly quickened pulse, justified laparotomy. I opened the abdomen an hour later and removed a 'normally' placed distended appendix, completely gangrenous and with a hard concretion, the size of a green pea firmly impacted in the base. The history and symptoms of this case tell the story of the pathology chapter by chapter.

I. At that early hour of the day when life is at its lowest ebb and unstriated muscle at its most irritable, the expulsive efforts of the appendix impact the stone firmly in the base. II. The efforts are now redoubled, causing sudden severe colic, awakening the patient and stimulating the vomiting centre. III. The impacted stone cuts off the blood-supply to the appendix, which is thereby doomed. IV. The expulsive efforts of the dying appendix and the impulses carried by its dying nerves become feebler and feebler and finally cease, so colic and vomiting do the same, and the patient feels better. V. The dead appendix irritates the parietal peritoneum and causes local tenderness, while its toxic contents raise the pulse rate. VI. Operation. VII. Recovery. So the story has a happy ending because of the episode in

chapter VI, but had this episode been delayed by even a few hours, the appendix would have burst, and although the end of the story would have been more exciting it would have probably been tragic.

Shortly afterwards I saw a similar case, but the pain and tenderness were more vague and the pulse was 50. I put him to bed and ordered two-hourly pulse and temperature records; he was quite well next day and has remained so. He had indigestion.

It will be noted that in the second case even after some hours there was a lack of localization and a slow pulse, though this happened to be exceptionally slow. In spite of the textbooks I have found the pulse a most valuable guide in acute abdominal conditions. It is generally quickened in gangrenous appendicitis, but unfortunately not always. To sum up; gangrene of the appendix is an emergency of the first order, its symptoms and signs are few, but they include sudden severe colic and vomiting, generally a quickened pulse, and to the careful examiner who does not forget to examine the rectum, some localized tenderness. In doubtful cases a delay of two hours is permissible, but if there is still doubt it is wiser to operate. Most patients would rather have an operation than a post mortem.

Mention of delay and doubtful cases recalls the subject of leucocyte counts and other aids to diagnosis. How often does one see the inexperienced, undecided surgeon relying on them instead of on himself? A leucocyte count has its uses, the chief of which is to distinguish between an inflammatory condition such as appendicitis and non-inflammatory one such as ureteric colic, but a skilful clinician will generally make the distinction at the bedside, and it must never be forgotten that the most fulminating and gangrenous conditions may be associated with a normal white count or even with a leucopenia. Aids to diagnosis are not an excuse for lack of courage or lazy thinking and they have only a subordinate place in abdominal emergencies.

Recurrent appendicitis.—This is not the same thing as chronic appendicitis, and, as its name implies, it consists of a series of subacute attacks which leave behind them a varying amount of fibrosis or cicatricial contraction; progress and symptoms naturally depend on the tissues affected, for instance, a stricture of the appendicular wall does not produce the same pathological or clinical picture as morbid adhesions to the Fallopian tube. The beginning—or the end—of the disease may be an acute attack or even an abscess; fibrosis and adhesions are specially apt to follow the latter.

There is the further complication of concretions, which are frequent inhabitants of an appendix partly occluded by fibrous tissue. If these main conditions, namely, stricture, adhesions and concretions, either alone or combined, are borne in mind it is often possible to visualize the pathology from the symptoms.

In simple stricture any flare up is likely to prove serious because of the risk of appendicular obstruction and consequent gangrene, although in recurrent cases the omentum can often prevent a cataclysm. Adhesions most commonly cause binding down or kinking of the appendix, with consequent partial obstruction and attacks of colic. At different times I have found the appendix adherent to the liver, the small intestine, the large intestine, the ovary, the pre-sacral nerve, the uterus, the Fallopian tube, the ureter, the bladder and the sac of a hernia; from which diverse lesions it will be easily realized that a variety of symptoms can occur.

The presence of concretions gives rise to the very common symptom of appendicular colic; the organ naturally tries to—and often does—get rid of these unwelcome intruders, so it goes into paroxysms of peristalsis in order to do so, arousing the characteristic sensation of colic and nausea; it seems probable that, through vagus and sympathetic stimulation, appendicular colic also causes a certain amount of gastric and duodenal disorder, but this is more characteristic of true chronic appendicitis, to be discussed in the next section.

When an acute attack supervenes on a 'recurrent appendix' the question of treatment may be extremely difficult to decide and, even if the surgeon thinks that conservatism is indicated, it may need more courage for him to hold his hand than it would for him to operate. In these cases one's thoughts generally run somewhat on the following lines:—

'The patient has survived previous attacks without operation, so will probably survive this one; there must be adhesions round about, which will localize any inflammation, so a peritoneal disaster is not likely; I think I'll wait, and remove the appendix in a few weeks' time. . . . On the other hand, a fibrotic appendix is more likely to get obstructed than a healthy one, so it may go gangrenous or rupture, and of course in a couple of months' time he'll say he is perfectly well, so he may refuse operation. . . . I think I'll examine him again.' In India there is the further difficulty that if a doctor gets a name for advising operation, his patients are apt to seek advice elsewhere, and we all know the patient who at the mere mention of an operation 'Must ask my relations'; which means that he goes off to another practitioner—generally unqualified—who gets the credit if he recovers. If not, the patient often comes back praying for operation when it is too late, as no wise surgeon will open a hopeless abdomen.

The problem may be made easier by the fact that these recurrent cases often call one in after the worst is over, 'because I've had these attacks before, but they've never lasted so long as this, do you think it might be appendicitis?' The indications for delay and an outline of the Ochsner-Sherren treatment have already been given, so need not be repeated. On the other hand, the problem may be more serious, because

'This is the worst attack I've ever had, doctor,' says the patient, and promptly hiccoughs, retches or vomits, all signs of peritoneal involvement, and consequently calling for operation.

Many cases lie between these extremes, and a knowledge of the principles already outlined, together with a clear visualization of the pathology and its probable progress, form the best guide to treatment. We therefore see that a good surgeon must be a good pathologist, a good physician and something of a psychologist, so that he can judge every case from every point of view. But a recurrent appendix must come out before the next attack.

Chronic appendicitis.—All surgeons and some pathologists can find something wrong with an appendix that has been removed, but the pathology is complicated by the fact that as years go on the appendix tends to fibrose, and Keith states that by the age of 70 half mankind have a fibrotic appendix.

Although some gastro-enterologists are beginning to question the existence of true chronic appendicitis, perhaps as a swing-away from their former over-incrimination of a frequently innocent organ, there are two distinct types of true chronic inflammation, which might be called the atrophic and the hypertrophic. The former, as just pointed out, is more or less physiological for about half of humanity; it begins at the tip and works to the base. When doing a hysterectomy or other abdominal operation on a patient over 50, I have several times found the tip of the appendix fibrotic and the rest of the organ normal, but I have never had the chance of seeing the same appendix years later. If I had, I should probably have found the whole organ fibrosed. Clinically the condition is not important though it may give rise to some dyspepsia and may, of course, be complicated by other lesions. It is my practice to remove an appendix whenever I see it atrophic.

The hypertrophic type is much more interesting. It occurs in younger people, in my experience more often in women than in men, and is often retro-cæcal. The tip of the appendix is frequently bulbous and tender and there are no morbid adhesions to other organs. The essential lesion is a chronic inflammation of very low grade followed by a sort of hyperplastic fibrosis: it begins in the submucous coat and later involves the mucous and muscular layers, the lumen being occluded in the former case and enlarged in the latter. The process also affects the nerve plexuses of Auerbach and Meissner, which may proliferate very markedly (Masson), and it is a pleasing deduction that this is the cause of the symptoms, which are those of the cholecystitis or peptic ulcer type, but without relation to food. The pain is often brought on by exercise or mild constipation and may be accompanied by mental depression. On examination there is some tenderness over the appendix, masked if it is retro-cæcal, and pressure may evoke nausea. The diagnosis is best made by

x-rays and treatment is appendicectomy through an incision large enough to allow an exploration of the whole abdomen.

We therefore come to the following conclusion : In patients below 40 with persistent abdominal discomfort suspect the appendix, but do not condemn it without convincing evidence; in patients over 40 consider also malignant disease, especially if the symptoms are of recent origin.

Effects of position

Normal position.—The appendix is nearer the surface than in other positions, so physical signs will be clearer and more typical. Should perforation occur, general peritonitis is likely because the organ lies in the general peritoneal cavity. An abscess tends to point anteriorly, can generally be felt and may cause surprisingly few symptoms.

Retro-cæcal position.—This presents difficulties both in diagnosis and at operation, the cardinal sign of rigidity being neither frequent nor marked. As the appendix lies on or near the ilio-psoas muscle, rigidity occasionally manifests itself as a limp when the patient walks in. It can also be detected by the simple expedient of straightening the right leg, which is often kept flexed. A bi-manual rectal examination is of great help. It is a comfort to know that although a retro-cæcal appendix may be hard to diagnose it is not so dangerous as the other kinds because it is shut off from the peritoneal cavity. Should an abscess form it is generally lateral to the cæcum and may point in the loin.

Pelvic position.—On rectal examination, tenderness and perhaps a mass with lower abdominal tenderness are the cardinal signs, and in addition the patient may complain of dysuria, dyschesia or dysmenorrhœa if the inflamed appendix happens to involve the bladder, rectum, uterus or adnexa. In pelvic peritonitis low abdominal rigidity and tenderness may be accompanied by diarrhœa. It is dangerous to confuse the condition with ureteric colic and to waste hours or even days in accessory examinations. Once again, a careful enquiry into the why, when, where and whither of the pain, accompanied by a thorough clinical examination, which includes the rectum, will usually solve the problem. In cases of doubt an injection of 1/50th of a grain of atropin should be given; if the pain is due to ureteric colic the atropin will relieve it within half an hour, about the time it takes to get the theatre ready. Although urine examination should always be done, it is not so helpful as one might expect, because many cases of renal or ureteric colic show no obvious hæmaturia or other gross urinary change. It is perhaps worth remembering that a skilled radiologist with good apparatus can do a pyelography in less than an hour, though this is not advised as a routine procedure. If a pelvic appendix forms an abscess, it often points into the rectum.

Differential diagnosis

Acute appendicitis.—A temperature of 103 or over in an adult is against this although it does not exclude it, but pyelitis, diaphragmatic pleurisy, liver abscess, malaria or enteric is more likely, and that rather elusive entity known as gastro-intestinal influenza is always a possibility. The detection of pyelitis may be difficult, but apart from the urine changes and the symptoms there is generally tenderness in the loin on deep inspiration. Pyosalpinx can be distinguished because it is bilateral, there may be a vaginal discharge, and the educated fingers can feel the swollen tubes in the posterior fornices, but it may cause difficulty. Ectopic gestation is easily confused with acute appendicitis if there is no history of menstrual irregularity, but a boggy mass can usually be felt *per vaginam* and the patient feels pain when the examining fingers move the cervix—a most valuable sign. But the treatment is the same, laparotomy.

In patients over 50 the commonest causes of recent severe flatulent dyspepsia are coronary occlusion and gallstones, both of which are often accompanied by vomiting. The detailed diagnosis of coronary disease is beyond the scope of this already long paper, but it should be suspected if there is dyspnœa with retro-sternal pain, pallor and sweating. As already mentioned, gastric crises are rare in India.

Recurrent and chronic appendicitis.—As radiography is essential for accurate diagnosis of these conditions, it will be considered by Captain Galstaun, but amœbic dysentery, spastic constipation, tubercular peritonitis or adenitis (particularly in children), windy or tubercular cæcum, spinal caries, peptic ulcer, gallstones, jaundice, vomiting of pregnancy, cancer, and, finally, morbid interest in one's own insides have to be remembered. The last-mentioned can be diagnosed when the patient comes up with a written or (worse) a typed list of symptoms, with perhaps a sheaf of prescriptions and laboratory reports. These patients are often childless, but if the obvious remedy cannot be applied they may benefit by psychotherapy; further, they are often rich, so form a great temptation—and a frequent source of income—to the unscrupulous. From our present point of view, unless clinical and x-ray examinations give unequivocal evidence that the appendix is the cause of the trouble, and the patient can be convinced that it is, operation will benefit neither patient nor surgeon.

Complications

General peritonitis, sub-phrenic and pelvic abscess are obvious complications; further, infection may spread from the appendix to the lymph glands, which may form a retro-peritoneal abscess, or into the portal blood stream causing multiple abscesses in the liver (suppurative pylephlebitis). In one case of this that I saw, the tragedy was a double one, because the

patient's widow committed 'suttee'. Acute generalized septicæmia is a rare complication, although the appendix is often incriminated as being a focus of chronic sepsis.

In a mildly septic case, particularly in a fat person or a woman, the great care must be taken to prevent thrombosis of the saphenous, femoral or iliac veins. As it may cause pulmonary embolism the condition is a dangerous one. It should be suspected if the patient's temperature rises after the first week or ten days, and there may be some tenderness over the saphenous or femoral veins with perhaps œdema of the foot. Since abolishing the use of a pillow behind the knees for more than an hour at a time, making the patient move his legs as soon as he comes round and keep on moving them and his body several times a day, I have not seen a case. A simple appendix case can turn on his side within a few hours of operation. Femoral thrombosis is rare before thirty and almost unknown before twenty. It may be asked, 'What about the high Fowler position?' The answer is that the patient can still move his legs and turn partly on his side, and the pillow or Lawson Tait rest behind the knees can be moved, or replaced by a board put across the bed as a foot-rest.

Paralytic ileus deserves special mention because of its danger, its preventability and the fact that it is apt to affect the middle-aged, the well-nourished and the mildly alcoholic, in other words, the 'important' patient, whose demise may be as tragic for his surgeon as it was for himself.

Apart from this the ætiology is not certain, but ileus is likely when the appendicular inflammation has been severe and the peritoneal reaction marked, or when there has been much handling or exposure of the gut at operation. For several years now it has been my practice at all abdominal operations never to allow more than a few inches of gut to be exposed at a time, and since keeping carefully to this system, I have seen much less post-operative ileus; the old method of wrapping up yards of gut in a hot towel laid on the abdominal wall is an invitation to ileus that will often be accepted.

In patients of the kind described above, and whenever ileus is expected, 10,000 units of anti-gas-gangrene should be given intramuscularly on the table and repeated if necessary for the next two days. A laxative pill on the night of operation followed by a small enema in the morning also gives great comfort.

If ileus does occur, there is no need for panic, as most cases get well, the prognosis being good if the pulse remains below 90, but bad if it remains above a 100. If the symptoms come on early and suddenly, they may be due to acute dilatation of the stomach, the treatment of which is a gastric tube left in position for many hours, aspiration and lavage being carried out through it. Ileus should never be confused with obstruction due to adhesions or kinks, because ileus comes on within 60 hours of

operation, while obstruction does not begin until eight or ten days after operation.

In early cases of ileus, a full dose of eserine or prostigmine and pituitrin followed by an enema generally gives relief. Later treatment depends on circumstances and, as with secondary uterine inertia, is more likely to be successful after a rest of several hours under morphia and atropin. If the general condition is good and there is no nausea or retching, castor oil, with an enema four hours later, should always be tried before further measures are adopted; these are fully described in the textbooks, so need not be detailed here, the underlying principle being to reduce sympathetic and increase vagus activity by such drugs as acetylcholine, prostigmine and pituitrin, to combat toxæmia, to keep the patient supplied with fluids, to support the heart and not to 'flog the tired horse'. A spinal anæsthetic is a better and more logical last resort than enterostomy, which will seldom achieve what a rectal and duodenal tube cannot.

Treatment

Conservative treatment and its indications have already been discussed, so we need consider only a few points about operative technique. The incision is a subject of interest and controversy, so I give my own experience. Twenty-five years ago I was a sincere advocate of the McBurney muscle-splitting incision; finding that it gave a limited exposure, took rather a long time and could not be readily enlarged, I tried the Morison muscle-cutting incision, but was not satisfied that, for what generally proved to be a simple operation, it was necessary to inflict such trauma on the abdominal wall. I then started using Battle's para-rectal incision, which has the advantage of bringing one down on a 'normally' placed appendix. But the nerves to the rectus muscle cross it, so one may be cramped for room; cutting one nerve, usually the eleventh dorsal, does not seem to matter, but to cut more is to invite an incisional hernia from paralysis of the rectus. However, I used it for many years, and once even removed a left ovarian cyst through it. I then began to employ spinal percaïne or a really good anæsthetist, so obtained really good relaxation of the rectus muscle, since when I have found nothing to compare with the paramedian incision. It can be indefinitely lengthened without harm, it gives good exposure and it heals strongly. Should there be any inaccuracy in the diagnosis, it avoids the loss of time and reputation caused by making two incisions. As a rule it is unsuitable for a case of frank abscess, the incision being made where the abscess is pointing.

The actual removal of the appendix proceeds along classical purse-string lines, but it is unnecessary to carbolicize the stump, and in the 'interval' operation I first ligature the meso-appendix with the purse-string stitch, thus drawing it up to the cæcum and covering the raw area. Occasionally, with a long adherent

retro-cæcal appendix, it is easier to divide it first from the cæcum and dissect it out from base to tip. Most difficulties are caused by an inadequate incision or a bad anæsthetic. One of course takes advantage of what one hopes is a unique opportunity and examines the other viscera, dealing with any lesions found; the paramedian incision makes this easier.

While closing the wound I like to powder it, especially the subcutaneous fat, with thiazamide, and for sewing up the skin I have a weakness for a subcuticular stitch, which may have some psychological value, as a patient with a neat scar attributes it to a careful surgeon. Throughout the operation, indeed throughout any operation, gentle handling of tissues, perfect hæmostasis, and accurate approximation of divided structures must be observed, and will be rewarded by perfect healing. These are more important than speed, and the surgeon with one eye on the students and the other on the clock has no place in the modern operating theatre.

A final word about treatments with a name. Because of Ochsner-Sherren sulphanilamide, blood transfusion or some other treatment is fashionable, it does not follow that the surgeon has done all that is necessary if he prescribes it in the wrong case. Now, as always, treatment should be founded on knowledge and dictated by experience. Some forms of treatment come to stay, others are replaced by something better, and the rest survive only so long as faith in them endures.

When I was a student, the Sippey diet was considered a specific for gastric ulcer and the Weir-Mitchell treatment for neurasthenia. The latest edition of a famous textbook of medicine mentions neither of these names, but the index devotes a column and a half to vitamins. One wonders. . . .

Radiology in appendicitis

Indications.—Radiology is not to be thought of in acute appendicitis, and is but rarely needed in subacute cases, though in some instances, when inflammation of the uterine adnexa cannot be excluded clinically, an x-ray examination of the appendix may be helpful.

It is in cases of recurrent and chronic appendicitis, particularly those associated with chronic dyspepsia, that x-ray examination finds its fullest scope. The importance of a full radiological survey in such cases cannot be exaggerated. The gall bladder should be examined by cholecystography, the liver being screened *en passant*. On the following day a complete opaque meal examination can be done. It has been my experience in India that in a considerable number of the patients sent for x-ray examination for chronic dyspepsia, the symptoms are due to amœbiasis. The value of screening the liver is shown by the following case which I saw recently. Chronic appendicitis was suspected and the above routine carried out. On screening the liver I found it distinctly enlarged;

there was marked diminution in the movement of the right side of the diaphragm, with partial obliteration of the right costo-phrenic sulcus. The opaque meal showed some spasticity of the colon. Although the patient's stools were negative I suggested amœbiasis as the cause of this trouble. All signs and symptoms cleared up under emetine, and there is no doubt that x-ray saved the patient from an unnecessary laparotomy.

Preparation.—As a corked bottle cannot be filled, so an appendix with the proximal part of the lumen blocked with mucus or fæces cannot. The patient should have an aperient such as cascara evacuant or pulv. glycyrrhizæ co. the night before, and a hot (about 110 degrees Fahrenheit) high saline enema early on the morning of the examination. This *must* be efficient. Aperients that cause gas, such as castor oil, should not be used.

Examination.—The stomach and duodenum should first be examined to exclude (or otherwise) peptic ulcer and duodenitis. Any other condition in this part of the bowel should also be looked for. Any of the well-known proprietary brands of barium emulsion may be used—they are all excellent. I have found no advantage in using such additions as buttermilk in the opaque food. In many cases this meal alone will fill the appendix.

The stimulus of epsom salts, one to four drachms in three to four ounces of water, according to the methods of Czepa or Cambies—the former in the meal itself and the latter two to three hours after (preferred)—makes filling certain in cases where the lumen is not obliterated, particularly when in doubtful cases the procedure is repeated. As already mentioned, it must be borne in mind that, after the age of 50, the appendicular lumen tends to stenose, so that non-filling in such patients is not a matter of the same importance as in younger subjects. A method popular in France is to use a smaller quantity of the opaque emulsion, 100 c.cm. followed by 2 c.cm. of castor oil. Its advocates claim this method to be as successful as the epsom salts method.

Whatever the method used, *the normal appendix should fill at seven hours, if not before*. At this time there is some meal left in the terminal ileum, so the ileo-cæcal junction can be studied. It may be necessary to eliminate such pathological states as ileo-cæcal tuberculosis, regional ileitis (Crohn's disease), or malignant disease.

The normal five hours' examination for stomach or duodenal residues should not be omitted. After this the patient should be given a pappy, bulky meal, such as spaghetti and a milk pudding. At ten hours the terminal ileum should be empty; this is referred to later. If the appendix has filled at this time, the patient should be further examined at 24 hours and for some time after the cæcum has emptied. If on the other hand the appendix has not filled, then a

second meal should be given. In rare cases a third one may be necessary at 24 or 36 hours.

The importance of varied and adequate compression (German 'Dosierte kompression') in examination of the cæcal region and appendix cannot be overstressed. I have often seen cases in which, without such compression, the appendix would not have been visualized, but in which and with such a compression, a beautiful delineation has been obtained.

A properly designed compressor will usually enable the radiologist to separate the appendix from overlying bowel. Because of the case with which the patient can be rotated to any requisite position, it is usually convenient to examine opaque-meal cases in the erect posture, but in examining the appendix, particularly when the cæcum is low, it is often necessary to have the patient supine.

Radiological signs.—These may be divided into direct and indirect.

Direct signs.—Of the normal filled appendix the shadow is usually 8 to 10 cm. in length and 2 to 4 mm. in width. It is nearly always curved in some direction. A retro-cæcal or pericæcal appendix should be searched for, and any variation in length or calibre looked on with critical eyes. Anatomical variations or non-rotation of the gut or non-descent of the cæcum may cause abnormal positions of the appendix. I recently had a case of inverted cæcum in a heavily-built patient; the appendix was at the upper end of the cæcum, lying transversely and adherent to the posterior abdominal wall above the umbilicus. Foreknowledge of this odd circumstance was of inestimable help to Colonel Williamson when he came to remove the appendix.

Except for some constriction normally seen proximally which is *not* pathological, the lumen should be regular. Other irregular constrictions or kinks should be noted and duly judged. A bulbous, Indian club type of tip is not normal. If definite, it is always pathological. A filiform appendix usually means constriction consequent on chronic inflammation. The presence of soft concretions, though in itself not important, becomes so when indicating bulges in the normal contour. In this connexion it must be stressed that irregularity of the lumen, to be of diagnostic value, must be constant. Such irregularities may be due to peristalsis, which can be watched, the observations being helped, if need be, by palpation and taking a series of small skiagrams. If the irregularity is due to stenosis, or to a necrotic or inflammatory bulge, it will be constant. Before the advent of pyclography, I once examined a case with a shadow the size and shape of a date stone in the right iliac fossa, in the position of the right ureter. The patient's symptoms suggested renal colic, but at operation the calculus was found in the appendix. Peristalsis is seen in the appendix; if not, the cause must be looked for. Delay in emptying, after the cæcum is empty,

is considered by French authors as a sign of prime importance in chronic appendicitis, the reason being a fibrosed wall. On the other hand, segmentation of the meal in the appendix is usually the result of peristalsis and is of no importance *per se*.

The normal appendix should be mobile. Occasionally such mobility may be restricted as the result of a short mesentery. Fixation at the tip, or definite kinks, suggest adhesions. Very rarely one sees the 'controlling' appendix of Arbuthnot Lane, where the appendix is adherent across the terminal ileum, fixing it down to the posterior abdominal wall and causing ileal stasis or even obstruction. A common adhesion is between the terminal ileum and the inner border of the cæcum, with the appendix somewhere in the angle between the two. Appendicular inflammation here would tend to spread to the peritoneal coats of both. Tenderness directly over the appendix is important, but it must be carefully checked by comparison with other sites.

Indirect signs.—Non-filling of the appendix when the technique has been properly and persistently carried out, in subjects below middle age, must be regarded with considerable suspicion. I have, however, searched for appendices which, unknown to the patient, had been removed, and, conversely, on three occasions I have seen perfectly-filled appendices which had been 'removed'. The lady owner of one of these was most indignant at my discovery and took a deal of convincing.

McLean of Glasgow, followed by Harnett and myself, has shewn the importance of a ten-hour residue in the ileum after the five-hour 'motor' meal of a bulky nature. This positive gastro-ileal reflex, while not definitely pathognomonic of appendicitis, is strongly suggestive of some intra-abdominal chronic inflammatory process. It was present in 98 out of 101 cases in my series, proved at operation.

Though this ileal stasis may be due to mechanical obstruction by bands of adhesions over the terminal ileum, it must be regarded in the majority of cases as a reflex phenomenon. The purely gastric stasis described by Barclay in these cases cannot be said to have the same value, as it may have other causative factors, even habitus.

In the absence of a filled appendix, fixation of and tenderness over the *caput cæci* are of diagnostic value, as is an easily elicited cæcal spasm.

The dysenteries may cause considerable confusion in diagnosis. Any case with proved dysentery, or radiological appearances in the colon suggestive of dysentery, may show either a non-filling appendix due to spasm or to mucus in the lumen, or that type of appendix seen when dysenteric catarrh has caused irregularity of the lumen. Such an appendix may also be tender on pressure. It is difficult or even impossible

to differentiate such signs from those due to appendicitis *per se*, so the radiological diagnosis will be in doubt. In such cases, unless the appendix is incriminated by overwhelming clinical evidence, it should be spared. When there is real doubt and the case is not acute, laboratory and therapeutic (e.g., emetine) tests may decide the matter.

It will be obvious that radiological evidence in chronic appendicitis, as in many other diseases, must be carefully weighed with all the other findings, clinical and laboratory. It is only by such consideration that a correct opinion can be arrived at, and that confession of failure in diagnosis called 'exploratory laparotomy' avoided.

Medical News

WOMEN'S BRANCH OF THE I.M.S. GRANT OF COMMISSIONED RANK

In their *communiqué* dated 13th January, 1942, the Government of India announced their decision to recruit women medical graduates to the Indian Medical Service with relative rank only. They are now pleased to announce that officers so recruited will be granted Commissioned rank from the date of their appointment in the Indian Medical Service in the same way as other officers of the service.

be appointed in the rank of warrant officers, class I, on a pay of Rs. 100-10-130, *plus* free single quarters (or compensation in lieu thereof), free furniture, conservancy water and lighting and free rations as for Indian troops.

Persons already in government service who volunteer for service as laboratory assistants or radiographers may draw the civil pay of their substantive civil appointment, *plus* 25 per cent of that pay as a compensatory allowance while serving in India and 50 per cent when serving overseas, in lieu of military pay and allowances, if the former are more favourable.

THE MEDICAL PRACTITIONERS' CO-OPERATIVE SOCIETY, LIMITED, BOMBAY

This Society is a Co-operative Society, which was started at the outbreak of this war, because of the extensive profiteering and adulteration in drugs that was taking place in Bombay.

They supply medical requisites to the members of the medical profession, at prices fixed according to the by-laws of the society and in consultation with the assistant registrar of co-operative societies without any profiteering or adulteration.

We have recently received a copy of the proceedings of the last annual general meeting. There are 250 doctors as shareholders of the society.

GRATICULES

In many types of measuring instruments mechanical methods in which vernier and micrometer scales were employed are now being replaced by optical methods in which the standards of measurement are provided by graticules. These are the cross-lines seen in surveying telescopes and other instruments. This replacement has largely been made possible by the development of special photographic methods in the laboratories of the British Scientific Instrument Research Association for the reproduction of graticules, and accurately divided circles bearing circular measuring scales.

Prior to the development of these methods it was necessary to rule each circle or graticule individually. This ruling was carried out by means of a diamond on the uncoated glass surface, or by a steel tool which cut through a layer of resistant material spread over the surface, thus exposing the underlying glass which could then be etched where the rulings had been made. Both these methods are subject to severe limitations. In the first place, by the ruling processes it is difficult to obtain lines with abrupt ends or to stop lines short at a point of intersection with another line. Under the high magnification to which graticules are subjected any gap or overrun becomes plainly visible. In the second place, a complicated graticule is exceedingly difficult to produce by any method of ruling and etching.

In the photographic method of graticule production a master of the graticule is drawn which may be a hundred times the required size. Sharp edges can be given to the lines of the master and all spacings can be accurately proportioned. From this master, reproductions can be easily and rapidly made with the elimination of all capricious and uncontrollable operations. One important feature of these graticules is that, although prepared by a photographic process, the transparent portions of the finished graticule are devoid of any film, thus eliminating the optical defects which arise in using ordinary photographic emulsions of silver halides in gelatine or collodion.

The use of the photographic process enables complicated graticules to be reproduced with ease, results in economy of production, and, as the processes involved are controllable, permits of a production time-table. When circles or scales so made are used for purposes of measurement, the brilliancy of the image seen, the opacity of the graduation marks against a bright background, and the large magnification employed, make it possible for readings to be taken with great ease and precision.

ABSTRACT OF THE MINUTES OF THE BENGAL COUNCIL OF MEDICAL REGISTRATION, DATED THE 11TH AUGUST, 1942

THE Council noticed with regret the delay in the amendment of the Bengal Medical Act and also the delay in the orders relating to the improvement in the Licentiate'ship course.

The Council noted that, as recommended by them at their previous meeting, the State Medical Faculty of Bengal was moving the Central Government for the inclusion of the M.M.F. qualification of the Faculty in the Schedule of the Indian Medical Council Act.

The Council approved the recommendations of the Special Committee to provide for extra students, under certain conditions, in the recognized medical schools other than those in Calcutta and Chittagong, with a view to provide against a falling off in the number of medical school students.

LABORATORY ASSISTANT AND RADIO-GRAPHERS FOR ARMY

(NEW TERMS OF APPOINTMENT)

THE Government of India have recently considered the question of an improvement in the terms of appointment of laboratory assistants and radiographers for the Army with a view to employing better qualified recruits. They have decided that, in future, candidates for appointment should be science graduates and should

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Public Health Section

PUBLIC HEALTH ORGANIZATION

VII. THE PUBLIC HEALTH LABORATORY

By RAJYASEVANIRATHA C. O. KARUNAKARAN

M.B., B.S., D.T.M. & H., D.P.H., D.B.

Superintendent, Public Health Laboratory, Central Research Institute, University of Travancore

In his introductory to this series Dr. Jacocks has stressed the importance of the public health laboratory as one of the four corner stones on which the modern public health edifice should be erected. After dealing in brief with the chief functions of the laboratory and other branches of public health, he has opined that the activities of each division could be elaborated into a full-sized paper. Having been engaged for nearly a decade in the organization and administration of a public health laboratory of the type outlined by Dr. Jacocks, which serves a State of six million people, the author hopes to deal, in this article, with the rôle of the laboratory.

'To-day in many health administrations, curative medicine and public health practice are so intermingled that it is difficult to distinguish the one from the other' writes Dr. Jacocks in his paper referred to above. In bridging the gap that was once growing wide between the preventive and curative branches of medicine, the laboratory has played a unique part. The history of the development of many a laboratory illustrates this. The King Institute of Preventive Medicine, Guindy, was, to begin with, the vaccine lymph depot under the sanitary commissioner with the Government of Madras, and, although other public health activities such as water analysis were introduced in 1905, it continued to function under the sanitary commissioner until 1922. Since then, it has been under the control of the Surgeon-General, but continues to serve the public health department just as it did before. The Pasteur Institute at Coonoor which was started for the preparation of rabies vaccine and its inoculation, has all along been under the management of the Association of the Pasteur Institute of Southern India and for many years now it has served as a public health laboratory in other directions as well. The Haffkine Institute, which began as an all-India centre for the study of plague and manufacture of plague vaccine, functions also as the provincial bacteriological laboratory for the Bombay Presidency. In Bombay, while this bacteriological laboratory is under the department of medicine, the Vaccine Institute (Belgaum) is under the public health department. In Mysore, where there are two separate laboratories, one for the preparation of small-pox vaccine and the other for other items of public health laboratory service, both are under the public health department. In Travancore, before the organization of the new laboratory

about nine years ago, there were four separate laboratories under different departments; a bacteriological laboratory under the medical department, a vaccine depot for the preparation of vaccine lymph under the public health department, a chemical examiner's laboratory for the examination of articles of medico-legal importance as well as for the analysis of water directly under the Government, and an entomological laboratory under the public health department. The new laboratory has been designed to provide adequate accommodation for the various independent activities in existence, and for their progressive expansion and the introduction of new activities. This laboratory approximates more nearly to the pattern outlined by Dr. Jacocks in his article and is perhaps unique in being the only institute in India which encompasses all laboratory activities in relation to curative and preventive medicine. The new laboratory functioned for some time under the public health department; but with the organization, three years ago, of a separate department for research under the young university of Travancore, it has become one of the important units of the group of laboratories belonging to that department. In spite of these administrative transitions, the service relationship with the different departments remains as before. It will therefore be seen that, although the services rendered by the various laboratories are more or less similar, their administrative position differs considerably and this fact illustrates how the laboratory more than any other institution has become the forum for the meeting of all persons engaged in the promotion of health, whether they be immediately concerned with the cure of disease or its prevention, or the planning of industry and trade.

One striking feature in the evolution of many of the laboratories is that almost all the older institutions were started for the preparation of some vaccine or other. As stated above, the King Institute was opened for the preparation of small-pox vaccine, and the Pasteur Institute at Coonoor for the preparation of rabies vaccine. In Travancore the laboratory for the production and distribution of small-pox vaccine was opened 53 years ago, while the bacteriological laboratory came into existence 25 years later. This sequence of events reflects in a general way the development of our knowledge of immunology and bacteriology. Jenner discovered his vaccine lymph and Pasteur his rabies vaccine long before the microtome, the high power microscope or the aniline dyes had made it possible to observe and to differentiate the various kinds of bacteria and viruses. The earliest of bacterial vaccines, the vaccines against anthrax and chicken cholera, were prepared by Pasteur long before the cultural methods and the biochemical and the serological

reactions, now of daily application in all diagnostic laboratories, were studied and standardized. Naturally the earliest laboratory service to secure public recognition and support was the preparation of vaccines. But bacteriology, immunology and biochemistry have made such phenomenal progress since the days of Pasteur and Koch, as has led to their extensive and every-day application in the fields of prevention and cure of diseases; and to-day a well-organized laboratory has little in common with the old vaccine lymph depot which probably served as its nucleus, in equipment, in staff and in the variety and vastness of its activities.

The work of the laboratory as has been briefly described by Dr. Jacocks is 'to supply an exact answer to many public health questions'. It provides the scientific basis for the control of all communicable diseases. Accurate and early diagnosis and specific immunization are the chief weapons in the fight against infectious diseases. The functions of the laboratory may therefore be considered under two main heads: (1) preparation of biological products, and (2) diagnostic service.

The preparation of biological products, the oldest recognized function of the laboratory, continues to maintain its premier position among the activities of many laboratories. Vaccination against small-pox had been known for centuries before Jenner discovered that cow-pox was modified small-pox and successfully used vaccine lymph to prevent small-pox. Jenner's vaccine was the first to earn scientific blessing and universal recognition. The number of biologic products now in use for the prevention, cure, and diagnosis of diseases is probably so numerous as to defy complete cataloguing. In general, they may be considered to serve three purposes: (a) the production of active immunity, (b) the production of passive immunity, and (c) the establishment of specific diagnosis.

(a) *The production of active immunity* is one of the most important methods of control applicable to many infectious diseases. The agent employed for this varies according to the nature of the disease. Where an anti-bacterial or an anti-virus immunity is to be produced, a vaccine is used, and where an anti-toxic immunity is desired, as in diphtheria or tetanus, a toxoid or toxin anti-toxin mixture is employed. The duration of the immunity conferred varies from many years, as in the case of small-pox vaccine, to some months, as in the case of plague or cholera vaccine. Active immunity has also found extensive application in curative medicine, and for this a large number of stock or autogenous vaccines and modified vaccines are in use.

(b) *Passive immunity* finds its main field in curative medicine. The various anti-toxic and anti-bacterial sera and the convalescent sera employed for producing passive immunity are all therapeutic agents of recognized value. Although generally used as curative agents, they have in some cases a limited prophylactic value, as in the

well-known use of tetanus anti-toxin in street accidents.

There is another group of biological products which, although of definite therapeutic significance, cannot be considered specific. The pooled human plasma and the hæmoplastic serum belong to this group.

(c) *The specific diagnosis* of infectious diseases involves the use of biological products of different kinds. The antigens used for determining the presence of agglutinins in the patient's serum, the immune sera for finally establishing the identity of a suspected organism isolated from the patient, the antigens and hæmolysin for complement fixation tests, the antigens for flocculation tests, the anti-sera for precipitin reactions, the antigens used for allergic tests such as the tuberculin test, or for determining susceptibility to infection, such as the schick toxin, all come under this category.

It will be seen from the above that the number of biological products used for different processes is so large that it will be outside the scope of any public health laboratory to attempt the successful and economic preparation of all of them. The main difference between a public health laboratory serving the State through the public health and medical departments and the commercial houses engaged in the preparation and sale of biological products lies here. The laboratory serves an area restricted administratively. Its purpose is to help the State in rendering free medical and public health service. It obviously cannot undertake competitive activities. The commercial houses have, on the contrary, a world-wide field. It is necessary alike for their prestige and their success that they should be able to meet all the requirements of their clientele in the sphere of biological products. All recognized biological products of standard quality are produced and made available to the public by the big manufacturing firms. Hence the primary consideration which should influence a State public health laboratory in undertaking the preparation and distribution of any biological product is that of cost consistent with quality. There are secondary considerations such as the prevention of loss of potency arising from transport from distant places, and the more satisfactory storage and distribution to suit local conditions and demands.

The evolution of this item of work in our public health laboratory illustrates this. When vaccination against small-pox was first introduced in the State, 78 years ago, the vaccine had to be purchased from outside. But for want of transport facilities, potency could not be maintained, and so the production of vaccine had to be begun here, 25 years later, although the demand had not yet reached a stage at which it was cheaper to produce than to buy. Since then, vaccination has been made compulsory and the demand has risen to such an extent that the cost of production is reduced to a fraction of the

cost at which the vaccine is available elsewhere. Now about 40,000 grammes of the vaccine are produced annually and the vaccine is supplied to the neighbouring State of Cochin also. Similarly, the increasing popularity of TAB vaccine and its extensive use by the public health department in controlling enteric fever during the last few years have been responsible for the preparation of this vaccine as one of our routine activities. Conversely, it may be stated that the preparation of the vaccine here and its free supply have contributed to its increased use.

Cholera vaccine, another of our major biological products, can be considered to have forced itself on us, under interesting circumstances. Eight years ago there was the explosive outbreak of cholera from which Travancore suffered as much as some of the badly affected areas in British India. Thousands of persons had to be inoculated daily. The King Institute of Madras from where cholera vaccine was being obtained could not meet the full requirements of this State. The new laboratory designed to provide for this activity was under construction, and the old bacteriological laboratory was meant to serve only as a diagnostic laboratory. But the situation made it imperative to take up the preparation of cholera vaccine. This was done, although it meant working in shifts, and in the course of six months cholera vaccine worth about Rs. 45,000, calculated at the rate at which the vaccine was being purchased, had been prepared and issued. We have had no epidemic of cholera since then, and the stray imported cases which have occurred now and then have necessitated the use of only a few thousand cubic centimetres of vaccine annually. Nevertheless, the preparation of cholera vaccine is one of the major routine activities of the laboratory, and besides keeping a sufficient stock to meet any emergency demand, suitable strains of the organism are periodically obtained from the Central Research Institute, Kasauli, or the King Institute, Guindy, and kept going so that the preparation of the vaccine on a large scale can be easily taken up the moment the call comes.

The preparation of rabies vaccine, the last of our major products, begun three years ago, had two considerations to back it up. The number of cases requiring treatment had progressively increased during the last eight or ten years to such an extent that the State was paying for this vaccine Rs. 10,000 to Rs. 12,000 annually. The new laboratory offered facilities for taking up additional activities, and naturally a biological product costing the State a considerable sum of money was an inevitable choice. Now this vaccine costs the State about 20 per cent of what it did before. Further, it is made available for agricultural live stock at a nominal price.

The cost of these four biological products, small-pox vaccine, TAB vaccine, cholera and rabies vaccines, supplied annually to the various departments of the State, calculated at the rates at which they are available in the market,

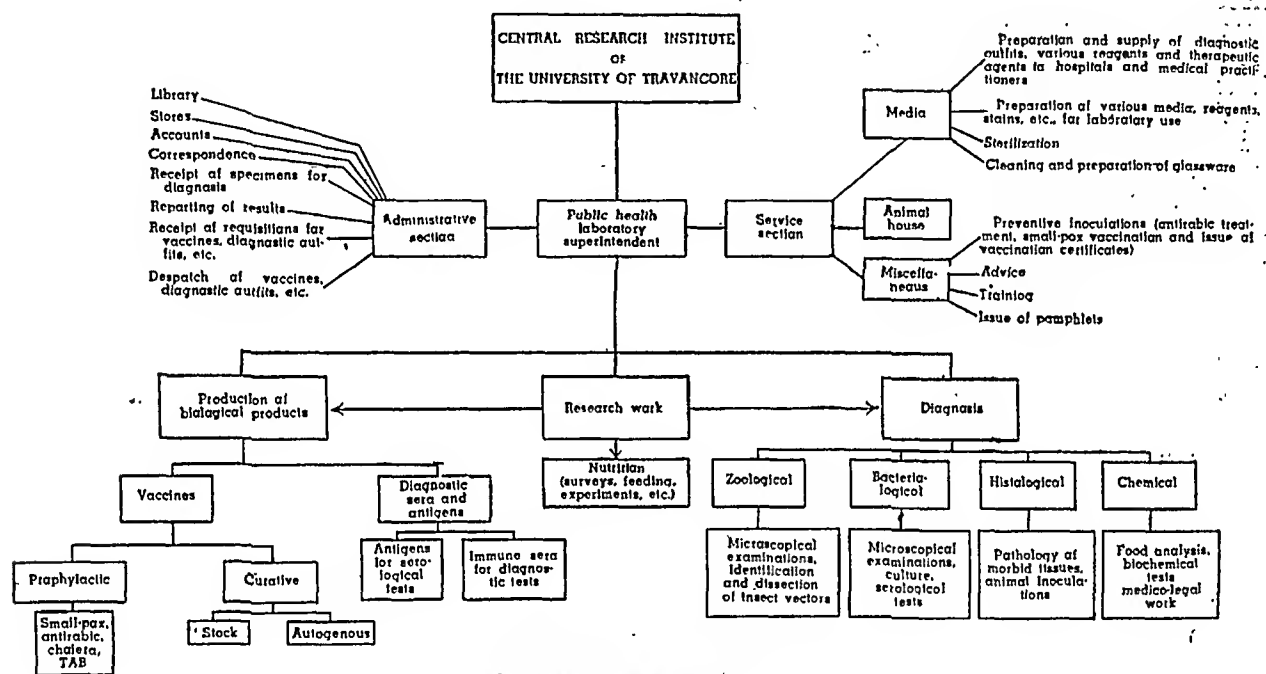
amounts to Rs. 40,000 to Rs. 50,000; and this covers fully the total annual budget allotment for the laboratory. It will therefore be clear that by a judicious selection of the biological products to be prepared, a State laboratory, serving a reasonably large administrative area—say, 5 to 10 million people—can not only pay for those activities, but also for its various other activities.

There are some subsidiary, but valuable, biological products, the preparation of which becomes easy as a result of the developments essential for the successful execution of major activities like the above. The development of a suitable animal house, an integral part of any scheme for the preparation of biological products, helps in the preparation of various kinds of diagnostic sera, and a self-sufficiency can be easily attained in this respect. We now prepare all the diagnostic sera including those used for precipitin tests in medico-legal work. Also, where provision exists for the preparation of prophylactic bacterial vaccines, it will not be difficult to meet the requirements of medical practitioners regarding autogenous and stock curative vaccines. The preparation of curative vaccines is not among the activities of the State public health laboratories in the United States of America. But there, all important hospitals have clinical bacteriological laboratories where curative vaccines are prepared. In India, on the other hand, few hospitals do their own cultural examinations, and the preparation of curative vaccine has to be done by the public health laboratories. Autogenous and stock vaccines for treating about 1,000 patients are prepared and supplied by this laboratory every year. There is another service that a public health laboratory can render with reference to biological products. It can obtain products of known potency and purity and stock them for distribution. For instance, the King Institute at Guindy buys various kinds of sera in bulk and dispenses them. This reduces the cost to a considerable degree.

Diagnostic service is probably of greater significance than the preparation of biological products. Early and accurate diagnosis is the basis of all control measures and is also of invaluable help to the clinician in the proper care of his patients. The vast majority of State public health laboratories in the U.S.A. do not undertake the preparation of biological products, because they can be readily had from private manufacturers at reasonable cost. Diagnostic work, on the other hand, would suffer in the absence of well-organized State laboratories. It is all the more so in India because most of the private medical practitioners and the smaller hospitals and dispensaries are without facilities even for ordinary microscopical examinations. The range of diagnostic service is therefore very wide, beginning with microscopical examination for the detection of the malarial parasite or tubercle bacilli, and ending with complicated cultural and serological tests or animal inoculations.

The number of diagnostic tests and techniques described or practised is so numerous that it will clearly be impossible to arrange for all these tests to be done in one laboratory. Serological tests for syphilis illustrate this point. Some laboratories do only the complement fixation test, others do the Kahn test, and many do both these tests. Here we also do a third test—Hinton's test. Still it occasionally happens that a medical practitioner who has read about some other test—say, the Meinicke test—inquires if that is not done here. Another writes asking if we do not do the Rubino test for leprosy or Craig's test for amœbiasis and so on. Results of their studies and observations are promptly published in journals by research workers. It is open to any laboratory to take up one or more of such problems for verification and, if found helpful, to adopt them as routine tests.

This subdivision is performed arbitrary and there is no water-tight separation between the sections. For instance, the section which isolates a suspected cholera vibrio does the agglutination test for establishing its final identity, and animal inoculation for determining the toxigenic potency of a diptheroid organism is done by the section which cultures the organism. Again, when the number of specimens under a particular group is large enough to necessitate the full-time work of one or more trained hands, special grouping may become necessary. For instance, during an epidemic of cholera when dozens of stools are received from different parts of the country, a separate sub-section for cultural examination of these specimens is useful. The number of specimens that we get from cases of enteric fever for agglutination and culture is generally so high that a sub-section formed as



Diagrammatic Scheme of the Public Health Laboratory in Travancore

That is how the so-called standard tests have emerged from trial to a position of general acceptance. But it will clearly be outside the scope of the routine service of a laboratory to provide for an unlimited number of tests, and preference will always be given to the more generally accepted tests.

The appropriate grouping of different items of diagnostic service will depend upon the volume of work under each item. In the case of this laboratory a broad division, on the following lines, has been found satisfactory.

Bacteriology.—This division has three sections, (a) serological tests including complement fixation, flocculation, and agglutination reactions, (b) microscopical and cultural examination of blood, stools, urine, sputum and other morbid exudates, and (c) histological study of tissues, and animal inoculation experiments.

an off-shoot of both sections (a) and (b) deals solely with this group of diseases. There are also items of bacteriological work, such as the bacteriological analysis of vaccine lymph which are done in the sections concerned with the preparation of vaccines.

Medical zoology.—Microscopical examination for malaria parasites, microfilariae, amœbæ and other intestinal protozoa, ova of helminths, etc., is done in this section. It also deals with the identification, classification and dissection, etc., of the insect carriers of disease.

Chemical.—This division includes three fairly well defined sections:—

(a) A public analyst's section is devoted chiefly to the analysis of food seized under the food adulteration regulations, but also undertakes the analysis of water, food, etc.

(b) A *chemical examiner's section* is engaged in the analysis of materials of criminological interest.

(c) A *biochemical section* for biochemical analysis, such as the estimation of blood- or urine-sugar; calcium, etc.

There are two items of service which follow more or less as corollaries to the activities discussed above. These are (1) research and (2) training.

Research.—In the preparation of biological products and the performance of diagnostic tests, problems are bound to crop up which require investigation and elucidation. Much of the progress made by bacteriology and immunology in relation to public health and curative medicine is the result of research done in various public health laboratories the world over.

A research outlook is a valuable attribute in every laboratory worker. It will help to improve his or her knowledge and make the otherwise dull and prosaic routine activities more inspiring and attractive. Every laboratory should therefore afford facilities for research. Research activities may be encouraged by appointing special research workers or scholars entrusted with specific problems; or by giving sufficient relief from routine work to persons normally engaged in that work. For concentrated effort, as in the case of urgent problems, one has to depend on special research staff; but everyone engaged in routine work should have sufficient leisure for reading and should be encouraged to study some problem connected with his work. A good library and periodic meetings of the workers are helpful to the growth of a research outlook and atmosphere.

Training.—A well-organized laboratory can and should afford facilities for training. Clinical laboratories attached to hospitals and field laboratories of the public health department require the services of trained technicians. Medical practitioners may also be in need of training in some particular branch of laboratory work. This laboratory has provision for training both these groups, the minimum general qualification prescribed for training as laboratory technician being the matriculation standard, but there is no difficulty in getting candidates having the B.Sc. qualification.

Miscellaneous activities.—These are certain services which a laboratory can conveniently render, some of which have an intimate bearing on the success of the main activities mentioned above, while others can be profitably taken up utilizing and supplementing if necessary the facilities which all well-organized laboratories possess. For instance, accuracy in diagnostic service demands that specimens should be carefully collected using appropriate diagnostic outfits. The preparation of these outfits is therefore one of the duties of the media section of the laboratory. The sterilization work and sterility tests daily done in this section can be

utilized for preparing and dispensing various substances used for injection either as therapeutic agents or for local or spinal anaesthesia. A considerable amount of work of this type is done by this laboratory.

The vaccines produced being always available in a fresh condition, the laboratory can provide for giving preventive inoculations. In addition to the treatment centres attached to the various hospitals, we have a centre for anti-rabic treatment in the laboratory. Vaccination against small-pox, cholera and typhoid is also provided for. While serving the public, this arrangement enables us to watch directly the reaction and results following the use of our biological products. Incidental to this is another line of service—that of giving advice both to the members of the medical profession and to the public on a variety of matters directly or indirectly related to the use of vaccines and sera.

Nutrition work.—A suitable animal house and provision for chemical and biochemical analyses and histological studies which are available in all modern laboratories furnish the requisites for taking up nutritional investigations. The Nutrition Research Laboratory at Coonoor has grown up almost as part of the Pasteur Institute. If sufficient accommodation is available, there appears no valid reason why nutrition work should not constitute an important feature of every public health laboratory; and in the case of small administrative units like ours, this arrangement has much to commend it. We have now a nutrition section in this laboratory. It is the youngest of our divisions. Its activities include diet survey and feeding experiments in the field and biochemical investigations and animal experiments in the laboratory. Two research scholars of the Travancore University are now working in this section, and this has been made possible by the present position of the laboratory as one of the constituents of the Central Research Institute of the University of Travancore.

Organization and administration.—As stated already the administrative position of public health laboratories varies from place to place. This laboratory is perhaps unique in being administratively connected with a university. The organization of the laboratory may be seen from the diagrammatic scheme given at the end.

The strength of the staff and the division of the staff into sections will depend upon the variety and volume of normal activities. This laboratory has a normal staff of nine officers, six of whom are medical men with special training in laboratory work, two chemists, and one medical entomologist. They are assisted by 10 laboratory assistants and eight junior technicians. There are five clerks and 20 menials. Research scholars assist in the study of special problems, and additional staff is engaged temporarily when pressure of work needs it. The laboratory deals directly with the various departments of the State. Departmental service is free. Service

is also free where the attending medical practitioner, including private practitioners, certifies that 'the party is too poor to pay'. Ninety-nine per cent of the service rendered by the laboratory is free. In the matter of the levy of fees for services rendered to persons who are not certified poor, this laboratory has followed the example of leading provincial laboratories, such as the King Institute, Madras. But this practice is at variance with that which obtains in the U.S.A. where the State laboratories render free diagnostic service in all cases. An argument that is often advanced against free State service is that it will impede the development of private diagnostic laboratories and put a severe strain on the resources of the State. While the validity of this argument cannot be denied, the reverse has also to be considered, i.e., that the payment of a fee, however small, will naturally put a check on laboratory diagnosis, which is bound to react adversely on public health measures. The goal that is placed before this laboratory is free diagnosis in all infectious diseases, and a step in this direction has been taken by 25 to 50 per cent reduction of the fees collected from the 'paying patients'.

The services rendered by a laboratory cannot always be evaluated in terms of money. The research schemes, the nutrition investigations, the preparation of various substances supplied by the medical department into sterile injectable products dispensed in appropriate containers, the supply of diagnostic outfits, etc., have no basis for computation as cash. If only those activities for which a scale of fees has been prescribed (at the lowest known rates) be taken into consideration, the services rendered by this laboratory are found to yield a 200 to 300 per cent return on the annual budget allotment. This will apply to every public health laboratory to a greater or less extent. A well-organized public health laboratory, in addition to being indispensable to the modern public health programme, is also an economic asset to the State.

Summary

The importance of the laboratory in preventive and curative medicine is briefly discussed. The growth, development and present position of the Travancore State Public Health Laboratory is outlined. A diagrammatic scheme showing its organization and operation is given.

Current Topics

The Use of Fresh Milk in Infant Feeding

(Abstracted from the Recommendations of a sub-committee appointed by the Indian Research Fund Association, May 1942)

Now as a result of the war dried powders are becoming scarce and very expensive. It is desirable to conserve the stock of dried milk for use where fresh milk is unobtainable and for times of emergency. Parents are therefore being asked first of all that no infant should be weaned unless it is absolutely essential and, secondly, that if artificial feeding has to be given and fresh milk is available, it should be used in preference to dried milks.

Immediately on receipt the milk must be boiled. After boiling it is important to get it rapidly cooled, and ice should be used for this purpose whenever possible. The milk should then be stored in a cool place and be kept at a low temperature. Where ice is not obtainable the hot milk should be poured into a cold jug, previously boiled and stored as recommended, standing in an earthenware dish full of cold boiled water, and a thin cloth soaked in cold boiled water should be placed over the jug dipping into the surrounding water. The dish containing the jug should be stood in a breeze so that cooling may take place by evaporation. When it is necessary to add water to the milk, the measured quantity of cold water previously boiled can be added at once to aid the cooling process. It is difficult to keep fresh milk good in really hot weather. Again a goat on the premises which could be milked when required might be the solution of this very real difficulty.

The first and most important rule to remember and act on is that an infant requires 2 to 2½ oz. of milk for each pound of body-weight every 24 hours. That is to say, a baby weighing 6 lb. needs 12 to 15 oz. of milk in 24 hours.

The second important rule to remember is that artificial food needs supplementing. The most important addition is vitamin C. The artificially fed

baby should be given fruit juice from the age of 5 weeks. Orange, papaya and tomato juices are good. Begin with three teaspoonsful and increase to 2 oz. Where the baby lives in the open air and gets plenty of sunlight the addition of vitamin D is not essential. Where sunlight is deficient it is very essential. Cod-liver oil or shark-liver oil can be given to supply this vitamin. They also supply vitamin A. Begin with 5 drops of cod-liver oil three times a day and increase to 1 teaspoonful at the third month and two teaspoonsful during the day at the sixth month. Shark-liver oil may be either pure or diluted with groundnut oil. If pure oil is used half the quantity recommended for cod-liver oil is sufficient; otherwise the same quantity should be given. Artificial feeds may also be deficient in iron and it is well to begin giving additional solid foods earlier to the artificially fed than to the breast fed baby. Foods rich in iron are yolk of egg, green vegetables and dals. Boiled water should be given in addition between feeds, particularly in dry hot weather.

Below are given suitable tables for the feeding of an infant during the first six months of life. The quantities given are for 24 hours. If a fridaire is available the whole quantity can be prepared at once and stored, otherwise half can be made in the morning and half in the afternoon. The sugar should be added just before the feed is due and before warming the mixture.

Fed on either of the mixtures A or B in the table below with the additions noted the baby will get a food sufficient in quantity and quality. The stronger mixture (A) is preferable and should be given if the child can digest it.

Buffalo milk may be used where cow or goat milk is not available. Buffalo milk is richer than cow's milk and greater dilution is therefore necessary. Suitable formulæ are given in the following table. Additions of sugar, vitamins and solids must be made as in the cow's milk formulæ and the same precautions to prevent contamination are essential. Water to drink between feeds is necessary.

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4. No undue irksome post-injection restrictions.

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Supplied in ampoules of 6 c.c.

THIOSTAB

A sterile aqueous 10% solution of Sodium Thiosulphate.

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Dosage tables are available on request

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MANUFACTURED BY:
BOOTS PURE DRUG CO. LTD. NOTTINGHAM. ENGLAND

Cow's or goat's milk

Age	Weight of baby	Formula A	Formula B	ADDITIONS		Calories supplied in formula A or B
				Fruit juice	Cod-liver oil	
First 2 weeks.	6 lb.	Milk 7 oz., water 7 oz., cane sugar 5 level teaspoons. Divide into seven feeds of 2 oz. each.				240
Second 2 weeks.	7 lb.	Milk 10 oz., water 8 oz., cane sugar 6 level teaspoons or 1 oz. Divide into six feeds of 3 oz. each.			5 drops	320
Second month.	8 lb.	Milk 14 oz., water 7 oz., cane sugar 6 level teaspoons or 1 oz. Divide into six feeds of 3½ oz. each.		3 teaspoons	20 drops	400
Third month.	10 lb.	Milk 18 oz., water 6 oz., cane sugar 6 level teaspoons or 1 oz. Divide into six feeds of 4 oz. each.	Milk 16 oz., water 8 oz., cane sugar 8 level teaspoons or 1½ oz. Divide into six feeds of 4 oz. each.	6 teaspoons	40 drops	480
Fourth month.	12 lb.	Milk 24 oz., water 6 oz., cane sugar 6 level teaspoons or 1 oz. Divide into six feeds of 5 oz. each.	Milk 20 oz., water 10 oz., cane sugar 10 level teaspoons or 1½ oz. Divide into six feeds of 5 oz. each.	1 oz.	80 drops	600
Fifth month.	13½ lb.	Milk 30 oz., cane sugar 3 level teaspoons or ½ oz. Divide into six feeds of 5 oz. each.	Milk 25 oz., water 5 oz., cane sugar 6 level teaspoons or 1 oz. Divide into six feeds of 5 oz. each.	2 oz.	100 drops	660
Sixth month.	15 lb.	Milk 35 oz. Divide into five feeds of 7 oz. each.	Milk 30 oz., water 5 oz., cane sugar 5 level teaspoons or 5/6 oz. Divide into five feeds of 7 oz. each.	4 oz.	120 drops	700

Should the child find it difficult to digest the buffalo milk mixture a doctor must be consulted.

Buffalo milk mixtures

Age	Weight	Formulae	Calories
First 2 weeks.	6 lb.	Milk 5 oz., water 9 oz., sugar 5 level teaspoons.	250
Second 2 weeks.	7 lb.	Milk 7 oz., water 11 oz., sugar 5 level teaspoons.	310
Second month.	8 lb.	Milk 10 oz., water 10 oz., sugar 5 level teaspoons.	400
Third month.	10 lb.	Milk 12 oz., water 12 oz., sugar 6 level teaspoons.	480
Fourth month.	12 lb.	Milk 15 oz., water 15 oz., sugar 7 level teaspoons.	590
Fifth month.	13½ lb.	Milk 19 oz., water 11 oz., sugar 4 level teaspoons.	650
Sixth month.	15 lb.	Milk 21 oz., water 13 oz., sugar 3 level teaspoons.	690

These formulæ need not be followed rigidly, but are given as examples of how milk mixtures can be prepared to meet the needs of the baby.

It is strongly advised that the baby should be weighed every week. He should gain 6-8 oz. weekly and if he is so gaining the feeding is satisfactory. Stationary weight indicates under-feeding or failure to digest. It is a serious sign and should not be neglected.

From 6 months onwards additional feeds should be given in the shape of solids and the quantity of milk

should not be increased. Towards 1 year of life if the child has learned to eat properly, the amount of milk taken can be gradually decreased from 2 pints to 1½ pints. During the second year one pint of milk should be sufficient.

On Amputation—Ten Commandments

By G. GORDON-TAYLOR

(Abstracted from the *Lancet*, Vol. I, 6th June, 1942, p. 669)

THE author, who is surgical consultant to the British Navy, offers the following ten rules which have suggested themselves as a result of the observation of nearly 3 years of war surgery. He states that the suggestions contained in these rules will not concern those who are charged with the duty of secondary amputation, but may be of value to those who have to undertake a primary or an emergency amputation, on an injured man.

1. A second expert opinion should always be sought, where possible, before amputating a limb, especially if it be the upper limb which is threatened with removal.

2. Anæsthetic.—In severe shock, spinal anæsthesia is certain euthanasia. Gas and oxygen is still the anæsthetic which is most likely to promote a successful result in the severely shocked patient or the 'desperate adventure'.

3. Tourniquet.—Apart from its use in first-aid work, the tourniquet is a barbarous mechanism with destructive potentialities. Where competent assistance is available for control of the blood-supply of the limb

to be removed, avoid a tourniquet altogether. Many years have elapsed since I have employed a tourniquet for a simple amputation.

4. Remember the long knife and do not be afraid to use it. The employment of a small scalpel to cut through the muscles and connective-tissue structures of a limb is ill-timed and unworthy bravado. The epic operators of the pre-anæsthetic days, famous by reason of necessity for dazzling speed and brilliant dexterity, paid attention to their surgical cutlery, length of blade and sharpness of steel. Amputation knives were forged and fashioned for a purpose. In the name of Heaven use them!

5. Nerves and Blood Vessels.—Cut through the nerves of the limb with the same circular sweep of the long sharp knife that sections the muscles. Do not add cruelty to your disagreeable task by pulling on, crushing or ligaturing the nerves or injecting them with alcohol. If it is possible to ligature separately from the nerve a bleeding artery coursing within the nerve sheath, take pains to do so. Every pull or insult to the nerve is an added pain to be borne. Blood-vessels are best ligatured with silk, linen thread or cotton. It is immaterial whether artery and vein are included in the same ligature or whether they are tied separately.

6. Hurry up!—The time taken to perform an emergency amputation should be reckoned in minutes and not in hours. The surgeon who spends the best part of an hour or more in performing any of the ordinary emergency amputations of war surgery has not only missed his vocation but wastes the time of his assistants, fails in his duty to his patient and

penalizes the chances of others who are awaiting surgical aid.

7. Transfixion.—In the direct emergency, when life is gravely threatened, speed can be further accelerated by transfixion-flaps, and the limb may be removed at the site of the fractured bone. This is a manœuvre only to be employed in the exceptional case, but its utility was proved from personal experience in the last war in the case of men who had been lying out in the shell-holes and the mud of Paschendaele, drinking their own urine.

8. Do not waste further time by putting a desperate case in plaster-of-paris for other injuries which may complicate a high amputation of the lower limb. A Thomas splint can be more rapidly applied and can be replaced by plaster subsequently, if this seems desirable.

9. Hæmostasis.—In the case of severe shock few vessels will require ligation, even in an amputation of the thigh, but oozing may take place later. It is therefore rarely advisable to suture the flaps closely without drainage; a piece of corrugated rubber drain at each corner for 24 hours will prevent a hæmatoma and certainly does no harm. If early transport is probable, it is important not to suture the flaps of an early amputation too closely; and if amputation has been delayed for more than 10 to 12 hours after injury do not perform primary suture of flaps at all.

10. Avoid massage to the stump like the devil.—The patient whose stump is massaged and who does not develop a painful limb must be under the special protection of Heaven.

Reviews

THE PRACTICE OF LOCAL ANÆSTHESIA.—By George Bankoff, M.D., D.Ch., F.R.F.P.S. 1942. William Heinemann (Medical Books) Limited, London. Pp. viii plus 198. Illustrated. Price, 17s. 6d.

THE realm of local anæsthesia has been fully explored by few surgeons, and the full extent of its possibilities is, in general, imperfectly known. This is no doubt partly due to the persisting demand of the patient to be 'put to sleep', adding thereby to the hazards which he may often be called upon to encounter. This book is an effort to bring the subject more into the light, and it is well written.

The work is divided into two sections, part I dealing with general principles and part II with their practical application. Of these the first is better than the second. It makes a very creditable effort in the discussion of the *modus operandi* of these drugs, their dangers, the choice of the agent to be used, and the technique of administration. One misses a definite statement of maximum dosages, one of the first things the inexperienced in these methods will seek. Auxiliary intravenous anæsthesia is included, and the whole section is well supported by bibliographic reference.

Part II is in many ways deficient, and its value could have been greatly enhanced by judiciously expanding certain chapters and eliminating others. The parts dealing with local anæsthesia in procedures involving the head and neck are well done and are amply informative, but thereafter the work 'tails off' and gives far too scanty consideration of procedures which are well tried, whilst bringing in others of doubtful value. For example, the use of 'local' in the setting of fractures receives but little space, and the chapters utilized for urology and gynaecology could well be omitted. There is a useful description of brachial block methods, but there must be few surgeons who would lightly distend the knee joint with the solution in dealing with a fractured patella. The suggested use of procaine alone in the bladder to desensitize its mucosa for suprapubic cystostomy and

prostatectomy shows a lack of experience in this work, and the extensive block described for a radical breast operation is quite unnecessary and success with a much simpler method is easily obtainable.

The effort to apply local anæsthesia to every possible circumstance is mistaken, and lightens the plea for its use when really indicated. Nevertheless, this work has a real value.

There are many valuable illustrations, though one wishes that most of the photographic diagrams had been more clearly reproduced.

C. M. S.

J. F. SUTHERLAND'S FIRST AID TO INJURED AND SICK.—Revised and rewritten by Halliday Sutherland, M.D. 44th Edition. 1942. E. and S. Livingstone, Edinburgh. Pp. 77 with 46 diagrams, one coloured. Price, 6d.; postage 2½d.

THIS minute booklet, measuring 4½ inches by 2½ inches, contains in a very condensed form most of the information given in the larger first-aid manuals. The book was originally written in 1887 and has now been rewritten by the original author's son.

The first sentence is a forbidding one—'The bones, 200 in all, omitting auditory ossicles and sesamoid bones, are divided into those of head, trunk, and extremities'. Why are auditory ossicles and sesamoid bones even mentioned in such a simple book on first-aid, and why talk about extremities? The rest of the book is not as bad as this, and on the whole is very clear and concise.

It is a pity that an English book on first-aid printed in July 1942 should not say more about air-raid injuries. The notes on shock are very brief and the crush injuries which have been so common are not even mentioned.

The index is useful, but rather unbalanced. The trapezoid, scaphoid and semilunar bones appear, but the femur is omitted. Even in this very small book, too much space is devoted to giving the Latin names even of unimportant things.

'Elastoplast' Dressing Strip for Lacerated Wounds



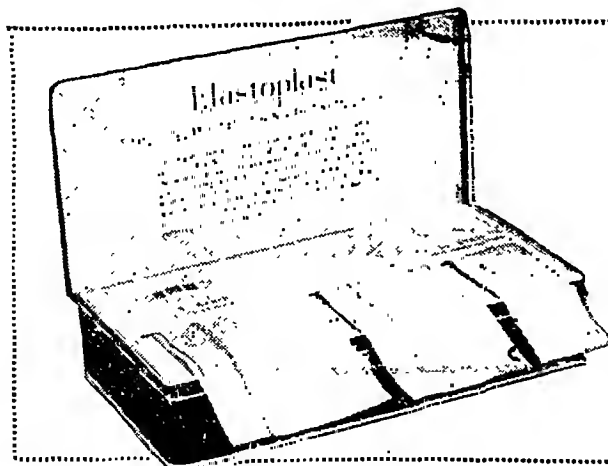
ON the 3rd February a patient attended with a $1\frac{1}{2}$ " laceration over the left eyebrow.

The wound was cleaned with peroxide, swabbed with flavine, and a piece of an 'Elastoplast' Dressing Strip applied so that the 'sideways stretch' approximated the skin edges.

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☆ The details above are of an actual case. The illustration is made from a photograph taken of this case. In the belief that such authentic records may be of general interest, the manufacturers of 'Elastoplast' are publishing these instances typical of the many in which their products have been used with outstanding success.



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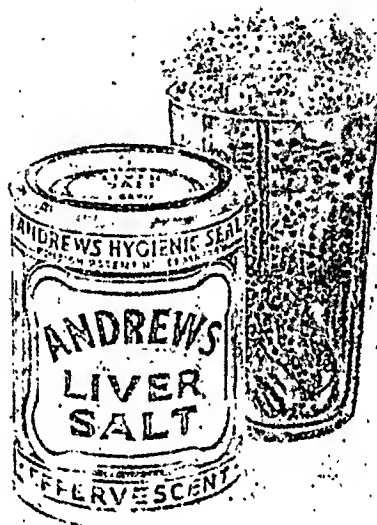
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5. Andrews creates no dependence on artificial aid, but can be discontinued when the need for it ceases.

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It certainly is an achievement to compress so much useful information into such a small compass and the book is certainly well worth its price, 6d. It would be difficult for anyone to learn first-aid from this book, but it might well be carried in the pocket or in the first-aid kit for ready reference by trained workers, and it might be used in revision before examinations.

VISUAL OUTLINE OF PSYCHIATRY.—By Leland E. Hinsie, M.D. 1941. Oxford University Press, London. Pp. v plus 109. Price, 12s. 6d. Obtainable from Oxford University Press, Bombay and Calcutta

THIS little book is part of an 'outline' series published by the Oxford University Press. Although definitely a book for students of medicine and therefore somewhat of a 'cram' book, it is nevertheless very well written and most up-to-date in the attitude adopted by the author towards psychological medicine and mental hygiene. Indeed, mental hygiene is the only subject to which perhaps less attention than is rightly due is paid since, so long as we are without a far greater knowledge of the causes of mental disorder and hence their treatment, mental prophylaxis is better calculated to enable us to reduce the number of patients yearly admitted into hospitals and sanatoria throughout the so-called civilized world. Perhaps because this book is written for students the author has permitted himself to dogmatize and nowhere hints at the general ineffectuality of medical practice as a whole for, excepting when hygiene has aided industry in promoting the growth of civilized populations, the influence of doctors on modern society has been sometimes beneficial, sometimes harmful, but always secondary. In no branch of medicine is this more evident than in psychiatry. The book is inter-leaved to afford blank pages for students to record notes on their own account.

O. B-H.

MATERIA MEDICA. PHARMACY, PHARMACOLOGY AND THERAPEUTICS.—By William Hale-White, K.B.E., M.D. (Lond.), M.D. (Dub.), LL.D. (Edin.). Twenty-fifth Edition. Revised by A. H. Douthwaite, M.D., F.R.C.P. 1942. J. and A. Churchill, Limited, London. Pp. x plus 502. Price, 14s.

To most medical men this book is an old friend. Dr. Douthwaite's preface to this edition states as follows—

'The new edition of this book incorporates the seventy-one important additions to the British Pharmacopœia that have appeared in the official Addenda II to V, issued since our last publication. The fifth addendum appeared too late for inclusion in the main body of work.

The subject-matter has been carefully revised and, in spite of extensive additions, it has been possible to reduce materially the size of the book. Saving of paper has been achieved by further pruning of sections dealing with pharmacognosy and those volatile oils which are still accorded official recognition. Furthermore, the publishers have skilfully made use of the page without detracting from its appearance.

As the result of the war many drugs have become scarce because they are imported, or because their manufacture requires materials used for other essential services. Lists of such drugs often used in the past are given. It is as important for the student as for the practitioner that these lists should be studied. A more complete guide can be found in the M.R.C. War Memorandum No. 3.

The section on sex hormones by P. M. F. Bishop is useful, as also is the chapter on the sulphonamides. The author points out that this term is a generic name covering all members of the group, that it is meaningless to refer to treatment by sulphonamides, and that the use of the word sulphanilamides as a generic name should be avoided.

The contents of a book of this kind are largely governed by the contents of the British Pharmacopœia. It must not therefore be taken as a criticism

of this book when one states that many preparations and drugs are included which one has never used and almost certainly never will use, either because their action is not definite and proved, or else because other drugs are much superior.

The book contains accurate information about the nature and the pharmacology of almost all drugs now in use.

On the therapeutics of tropical diseases, however, some questionable statements are made, such as the statement that tartar emetic is useful in the treatment of relapsing fever and yaws. It would be unwise for anyone to base their treatment of malaria on the information given in the book. The administration of thirty to forty-five grains of quinine about three hours before a malarial attack is due may kill the liberated 'spores' (*sic*), but how many patients would tolerate such a dose? Ten grains, four or five times a day between attacks, is far too big a dosage to be recommended; also the statement that intravenous injections of quinine should be given cautiously is not very helpful. The quinine should of course be highly diluted and given very slowly.

As a book on materia medica and pharmacy this book is excellent. The form, paper, and print are good. There are a few spelling mistakes.

PSYCHIATRIC DICTIONARY WITH ENCYCLOPÆDIC TREATMENT OF MODERN TERMS.—By Leland E. Hinsie, M.D., and Jacob Shatzky, Ph.D. 1940. Oxford University Press, London. Pp. vi plus 559. Price, 42s. Obtainable from Oxford University Press, Bombay and Calcutta

THIS is truly a monumental collection of words employed in a branch of medicine whose very existence is only beginning to be recognized. Some psychiatrists will be forced to laugh at many of the terms recorded in this dictionary, so bizarre are they in their ætiology, spelling and pronunciation. The number of words derived from or compounded with Greek words is so vast as to have led the authors to include a transliteration of Greek words. An idea of the comprehensive nature of this dictionary may be acquired from the following extract from the preface:

'A liberal use of cross-conferences, including the familiar *q.v.* and *see also*, and double registration of compound expressions under the main idea and under the modifying part, should make the book more serviceable, and search for desired information easier and more efficient. For instance, the impulse to buy is registered as *oniomania* and as *buy, impulse to*; excessive hunger is registered as *bulimia* and as *hunger, excessive*. Thus, a technical or scientific term which has escaped one's memory for the moment may usually be found under its popular English equivalent: *automatic action* is listed as such and as *paraphonic state* and as *action, automatic*.'

No hospital or practising psychiatrist should be without a copy of this valuable work.

O. B-H.

Abstracts from Reports

ANNUAL CLINICAL REPORT OF THE GOVERNMENT HOSPITAL FOR WOMEN AND CHILDREN, EGMORE, MADRAS, FOR THE YEAR 1941

THERE has been a remarkable increase in the number of cases treated in the antenatal section compared with previous years. The total number of deliveries during the year was 5,231, while that of patients admitted into the hospital was 13,453, the total daily average number of in-patients being 359.38. One thousand two hundred and twenty-five cases required artificial interference of some sort.

There were 3,161 cases of occipito-anterior and 999 cases of occipito-posterior presentations. Of the

occipito-posterior presentations, 121 cases were either persistent or malrotated occipito-posterior or cases of deep transverse arrest. Fourteen of these were spontaneously delivered, all children being born alive. In 53 cases, forceps was applied with traction and rotation combined, while in 46 manual rotation was first adopted and then forceps applied. Six of the cases were delivered with the occiput posterior, while in 2 craniotomy had to be performed. It may well be emphasized that in the large majority of cases, traction combined with rotation is adopted in the delivery of occipito-posterior positions. By so doing, the head is gradually rotated through the pelvic cavity till the rotation is completed almost at the outlet, thus imitating nature in its mechanism of delivery. In such cases, very little injury to the maternal soft parts is involved and the foetal head is not unduly compressed. Of the 53 cases treated, all the mothers were alive while 3 children were still-born and 6 died in the neo-natal period.

Cæsarean—classical or lower segment—and cæsarean hysterectomy have been the chief methods of delivery by the abdominal route. The lower segment cæsarean is only performed in cases of test labour when indicated and in cases where the woman has already been in labour for some time and the membranes have been ruptured and cephalo-pelvic disproportion is noted. The transverse curvi-linear incision is generally adopted in cases of delivery by the lower segment route. While the abdominal route has been resorted to in a fair number of deliveries, it is the practice of this hospital that, unless definite indications are forthcoming, the abdominal route is generally not encouraged. The more extended use of trial labour has resulted in the diminution of the number of cases of abdominal route delivery and the greater frequency of safe deliveries through the natural passages either by natural effort or by assisted labour. It need hardly be emphasized that the actual measurements of the pelvis are not a safe indication to judge of the probabilities of trial labour being successful and that a greater amount of importance has necessarily to be placed upon cephalo-pelvic disproportion, particularly after rupture of the membranes in a case of trial labour.

Internal podalic version has been performed not less than 43 times. In the majority of cases, this was done on multiparæ, and the indications varied from transverso and compound presentations to prolonged labour and slight degrees of cephalo-pelvic disproportion. It has been the experience here that particularly in multiparæ, where the head has still not engaged and indications for immediate delivery are present, it is a wise procedure to perform internal podalic version and deliver the child rather than attempt high forceps delivery. The results in such cases have been exceptionally good to the mother and, even from the child's point of view, afford better facilities for a live birth than by high forceps.

There were 30 cases of placenta prævia. Cæsarean section is the operation of choice in all cases of placenta prævia centralis while in the lateral and marginal varieties, Willet's forceps is applied more and more extensively after rupture of the membranes. The proper use of Willet's forceps in such cases deserves emphasis. The long Willet's forceps applied nearer the occiput region so as to favour flexion, getting in fact a good grip of the scalp tissue with light traction, has been found to be exceedingly useful and often results in labour ending by natural powers. Willet's forceps has also been used for other conditions such as cases of occipito-posterior presentations, cervical os and as a method of preventing a repetition of prolapse of the cord after manual replacement. Considerable emphasis is laid on the fact that vaginal examination in cases of placenta prævia should not be lightly undertaken and in fact, in severe cases of painless causeless hæmorrhage suggestive of central placenta prævia, the teaching at present is that such cases should preferably be examined with all preparations ready for an immediate abdominal route delivery, if the diagnosis

be confirmed, the patient being transported to the theatre before the vaginal examination is made.

There were 79 cases of accidental hæmorrhage. The majority of cases were of the mixed variety, i.e., both concealed and revealed. As is to be expected, in such a complication, still-births were common. Treatment of these cases of mixed hæmorrhage, consisted in rupture of the membranes and injecting small doses of pituitary extract, 1/6 c.cm. and plugging if necessary.

One hundred and forty-six cases were delivered as breech in the year under report. Three cases were delivered by lower segment Cæsarean section in two of which the breech was extended in primiparæ. Forty-five babies were still-born but this does not represent the corrected mortality. Twenty-four of the still-births were cases of macerated fetuses, while antepartum hæmorrhage, either accidental or unavoidable, was responsible for 8 cases of still-births, while in 6 others the still-birth was due to causes having no bearing on the breech delivery. It may be mentioned that the practice in this hospital is not to convert breech presentations into vertex presentations, but to conduct the delivery with due regard to the condition of the pelvis and to possible cephalo-pelvic disproportions maintaining the presentation as breech. It may also be stated that in a majority of cases, particularly in multiparæ, where the head is still above the brim of the pelvis or the greatest diameter has not passed through the brim and the dilatation is complete, if the necessity for interference should arise on account of signs of foetal distress, internal podalic version and extraction as a breech gives uniformly successful results and must be preferred to a high forceps application in the interests of both mother and child.

There were 17 cases of face presentation in 10 of which the mentum was posterior. Three children were still-born, one of which was a macerated fetus; one was delivered naturally and in only one case was perforation necessary. In the majority of cases, natural forces effected delivery. In two rotation and forceps succeeded in the delivery of a live child while in one case internal podalic version and extraction was done in a multiparæ.

Twenty-five cases of transverse presentations were treated with one maternal death and 15 still-births. In the majority of cases, internal podalic version and extraction was the usual mode of delivery. Decapitation and extraction was necessary in 3 cases when the woman came in with neglected shoulder presentation and with the foetal heart inaudible. Two premature babies, one of which was macerated, were delivered by natural forceps.

Compound presentations occurred in 16 cases, head and hand being the most frequent, head and foot; head, hand and foot, were also noted. Prolapse of the cord occurred in 4 of these cases. There were five still-births in the series.

There were 72 deaths out of 5,094 patients delivered at the hospital, 10 of whom were admitted in a moribund condition and died within a few hours of admission. It is worthy of note that a number of deaths were due to tropical diseases complicating pregnancy, anæmia, enteric fevers, tubercular disease and pyrexia of uncertain origin, these being responsible for over 25 per cent of the deaths. Rupture of the uterus occurred in 4 cases, while septic complications accounted for 22 deaths. The majority of these cases were cases delivered outside or handled badly elsewhere and brought to the hospital at a late stage.

There were 81 cases of eclampsia with 8 deaths giving a mortality of under 10 per cent.

ANNUAL REPORT OF THE EXECUTIVE HEALTH OFFICER OF THE CITY OF BOMBAY FOR THE YEAR 1941

The general conditions of public health of the city were satisfactory during the year. The number of live births registered during the year was more by 8,858 than the number of deaths that took place in the city. This excess of births over deaths was equivalent to 5.9

3 important medicines

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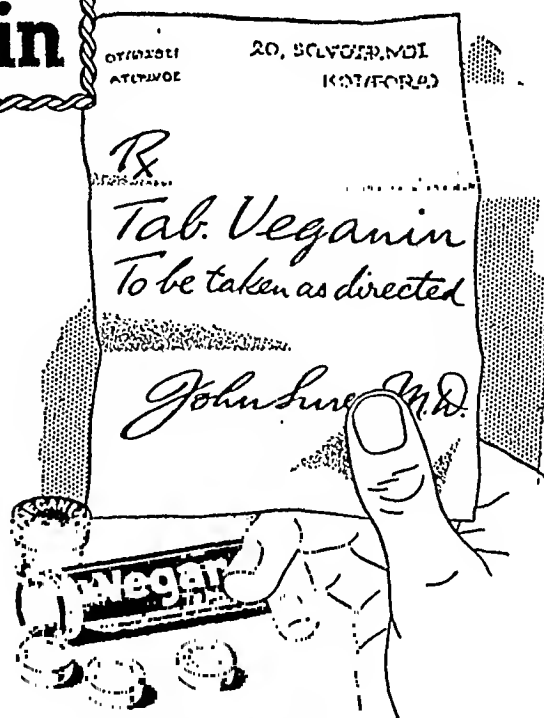
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per 1,000 population calculated on the census of 1941 although the actual number of live births was the highest recorded since the introduction of the registration of births and deaths.

The number of live births registered was 39,954 being 1,121 more than in 1940 and 5,759 more than the average of the last ten years (1931-40). The birth-rate calculated on the census of 1941 was 26.8 births per 1,000.

The total number of deaths from all causes was 31,096, being 1,996 more than in 1940, 168 less than the average for the last five years and 2,285 more than that for the preceding decennium. The death-rate for the year per 1,000 of the census population of 1941 was 20.9 as against 25.0 in 1940 and 24.8 the rate recorded for the decennium.

There was no death from plague during the year as against 14 the average of the last ten years (1931-40).

Smallpox caused 1,293 deaths as against 834 in 1940 and 889 the average for the last decennium. The disease was in an epidemic form from the 3rd week of January to the middle of May.

There were 7 deaths from cholera as against 6 in 1940. All cases were imported. The average number for the ten years was 14.

Influenza was prevalent in a mild form in the city during the year and caused 44 deaths as against 42 in the preceding year and 77 the average for the last decennium.

The deaths from diseases of the respiratory system numbered 10,186 being 745 more than in 1940 and 95 less than the average of the last ten years.

Tuberculosis accounted for 1,692 deaths as against 1,934 in 1940 and 1,841 the average for the preceding decennium.

Eighty-eight deaths were due to malaria, being 10 less than in 1940 and 13 less than the average of the last decennium. There were 668 deaths from ague and remittent fever as against 732 in 1940. The average number of deaths for the last 10 years from malaria was 101 and from ague and remittent fever 1,178.

The deaths among infants under one year of age numbered 8,445 against 7,823 in 1940 and 8,199 the average for the last ten years. The rate of infant deaths per 1,000 births registered was 211.4 as against 201.4 for the preceding year and 242.3 the mean for the preceding decennium.

Compared with the decennial average the total number of deaths shows an increase of 2,285, the principal increase in the mortality being 363 under congenital debility and premature births, 332 under old age, 266 under enteric fever, 37 under measles, 152 under violence, 26 under diphtheria and 20 under leprosy, 304 under smallpox and 27 under diarrhoea and enteritis.

On the other hand, there was decrease in the deaths under diseases of respiratory system by 95, under ague and remittent fever by 490, under dysentery by 15, under cerebro-spinal fever by 54, under influenza by 33, under puerperal state by 42, under tuberculosis by 149, and under malaria by 10.

Under a scheme for extending the maternity and child welfare services which was brought into effect from the middle of the year 1939, clinics are being conducted at each of the five maternity homes throughout the week. These clinics are no longer confined to ante-natal work alone, but ante-natal, post-natal and children's clinics are being conducted at each maternity home on two days every week, by the medical officer in charge thereof. Health visitors are appointed to work under the direct supervision of the medical officers.

There are five maternity homes maintained by the municipality. The total number of women admitted during the year was 6,509 as against 6,686 in 1940. The number of cases confined in the homes was 5,872 as against 6,223 in 1940.

The total number of schools visited by the inspectorial staff was 244 out of which 153 were boys' schools and 91 were girls' schools. The total number of children examined was 18,812 out of which 10,970 were boys and 7,842 were girls. Of these 10,011 children

(5,558 boys and 4,453 girls) were found defective on examination.

The principal causes contributing towards the insanitary condition of the city in some parts are the insufficiency of sewers, continuance of the basket privy system in unsewered areas, density of houses and persons per acre and inefficient methods of conservancy both as regards removal and disposal of refuse. With a view to accelerating the conversion of all the remaining basket privies into water-closets in the unsewered area, a subsidy is being given to the house owners since December 1939. During the year 1,007 basket privies were converted into water-closets.

With the completion of the Tansa pipe line, the city as a whole is now provided with an adequate supply of water from the Tansa Lake. The whole supply is chlorinated throughout the year. No provision of any kind is made for filtration.

The work of providing sewerage in the north of the island is now nearing completion.

During the year, one hundred and twenty-nine insanitary dwellings were evacuated and 307 huts were demolished and 458 rooms were improved. There are still many slum areas in the city which require prompt and immediate attention for their improvement.

ADMINISTRATION REPORT OF THE KING EDWARD VII MEMORIAL HOSPITAL AND THE SETH GORDHANDAS SUNDERDAS MEDICAL COLLEGE, BOMBAY, FOR THE YEAR 1941-42

THE 432 beds of the hospital (including the six beds recently added for the tonsil ward) were generally always occupied during the year under report.

Out of the total number of 13,564 in-patients (13,135 admitted during the year and 429 previous year's balance), 3,197 were cured, 6,870 were discharged relieved, 1,776 either left the hospital against medical advice or were otherwise discharged and 1,271 died leaving a balance of 450 patients at the end of the year. The highest number of out-patient attendance on any particular day during the year 1941 was 1,898, the highest number of new admissions in the out-door department on a single day being 517. Likewise the highest number on a single day of old cases treated was 1,334, of casualty cases 107 and of in-patients admitted 65.

The destitute and incurable patients of the hospital, as also those needing no active treatment but whose relatives would not take them away from the hospital were, as usual, sent to Lady Dhunba Jehangir Home for Destitutes and King George V. Infirmary for Incurables, respectively, which receive an annual contribution of Rs. 10,000 from the Municipal Corporation. Arrangements made with the Maratha Hospital and the Turner Sanatorium for the transfer of patients suffering from pulmonary tuberculosis were continued.

The number of mill accident cases has greatly increased this year as the number of such cases treated last year was 1,984 and 116 against 3,145 and 153 patients treated in the casualty department and admitted as in-patients, respectively, during the year under report. This may be due to the mills working double shift.

The treatment of school children attending the municipal primary schools was continued and 1,849 new children were treated in the different departments of the hospital. The total number of children treated in the year was 7,774 as against 8,637 treated in the previous year.

There were 80 new admissions into the college in June 1941. The number of undergraduate students on the college roll at the close of the year was 441, which included 74 lady students, and that of post-graduate and research students was 67.

The different departments of the college and the hospital had, in addition to their normal teaching, various research activities in hand during the year under report.

The Co-operative Credit Society of the labour staff of the hospital and college has been working satisfactorily and has continued to be in class 'A' since its promotion to it.

Correspondence

GRADING OF QUININE DOSAGE TO BODY-WEIGHT: POSSIBLE ECONOMY

SIR,—On account of the present urgent need for economy in the use of quinine the question of dosage for malaria is being widely discussed. It will be generally agreed that 'it is wise to calculate the dose per unit of body-weight whenever a powerful drug is given for the purpose of producing a full response' (Clark, 1935). Yet one has seen little reference to dosage of quinine expressed in terms of body-weight. Among large groups of men, such as soldiers who conform to known physical standards, minor variations in body-weight can be ignored and a standard course of treatment used. Among civilians there are much greater variations, but the same dose is often used. In this country, large sections of the population are normally of smaller build than, say, European soldiers. Most of those attending hospitals and dispensaries are under-weight from various reasons. Yet in the rush of work a full dose of the stock mixture or powder *t.d.s.* is often ordered, irrespective of whether the patient weighs 100 pounds, 120 pounds, or 140 pounds. Other circumstances being equal, if the dose is suitable for the latter case, it is obviously wasteful for the former. A saving of 20 per cent or more of the dose could often be made with no loss of therapeutic efficiency. Such a saving multiplied several million times would amount to a considerable total. Incidentally the same applies to most other drugs used in the dispensary.

For the wider application of this method, two things are necessary. Firstly, a personal weighing machine close beside the doctor where he works so that the patient has only to step on to it. Guessing the weight is less satisfactory, but an intelligent guess is better than ignoring the weight altogether. Secondly, the 'milligrammes per kilo' of pharmacologists must be translated into more familiar units. One way is to make the dose contained in one ounce of stock mixture suitable for a patient of 160 pounds and then give the one drachm for every 20 pounds body-weight. Or using the metric system with a full dose of 30 c.cm., 2 c.cm. may be given for every 10 pounds. In this hospital we use as a full dose 2 grains of quinine sulphate or totaquine per stone per day (20 mgm./kilo). The stock mixtures contain 2 grains per drachm, so a 10-stone man would get 10 drachms or 20 grains daily. Most of our adult patients are only between 6 and 8 stone, but formerly they were getting about the same dose. The dosage for babies and children is calculated in the same way. In any particular patient the dose may have to be modified for various reasons. Different scales of dosage may be adopted in different places to suit local conditions. But unless the dosage of quinine is graded according to body-weight it is impossible to assess the effects of variable factors in host and parasite, *e.g.*, individual or racial differences in response to treatment, due to immunity or tolerance on the one hand, and the virulence of local species and strains of parasite on the other. Nor is it possible to compare the results of those working under different conditions in different parts of the world. However our immediate concern is maximum efficiency in the use of the limited stocks of quinine available. It is suggested that a more general use of the method of grading of dose to body-weight would result not only in more accurate and scientific work but also in definite economy.

REFERENCE

CLARK, A. J. (1935) .. *Applied Pharmacology*. Fifth Edition, p. 12. J. and A. Churchill, London.

E. GORDON WILKINS.

MOORSHEAD MEMORIAL HOSPITAL,
BAPTIST MISSION,
G. UDAYAGIRI, GANJAM,
7th December, 1942.

DEATH FOLLOWING NEOARSPHENAMINE INJECTION

SIR,—I had a case of death within half an hour of neosalvarsan injection.

A Hindu male, aged 30 years, had asthma for the last six years. He was a compounder by occupation. He was given 3 to 4 neosalvarsan injections before for asthma with temporary relief. His heart had no organic disease, nor was he passing albumin or sugar in his urine. Every time he got an asthmatic attack, it lasted for three to four days. During the attack adrenalin injections used to relieve him but occasionally morphia had to be injected.

His last attack of asthma began on 4th December, 1942, and practically subsided by the 7th, and he asked me whether I would give him one neosalvarsan injection. A similar request was made to me a few months ago, but I had refused. This time I agreed and told him to bring the tube next day. No purgative was advised as his bowels were clear.

On the 8th he brought a 0.6 gramme tube of neosalvarsan. It was an old one but the powder was yellowish; no reddish coloration was present indicating chemical deterioration. I had used several old tubes like this before. The tube was not cracked. There was no paper cover with the tube, hence its date of manufacture was not known. The solution was made with boiled distilled water, and it was clear. He was injected at about 12-30 p.m. There was no untoward symptom during the injection. After the injection he was sitting on the table when he fell back. He was supported by the staff and I was called. I saw him immediately and found the heart failing. Adrenalin 1 in 1,000 was injected followed by strychnine and digitalin as the former had no effect. The patient died at 1 p.m.

I invite your readers to communicate their experiences, if any, of deaths after neosalvarsan injections and your criticism on the fatal accident.

C. G. MAHADEVIA, M.B., B.S.,
Medical Officer.

VERAWAL,
KATHIAWAR,
10th December, 1942.

[Note.—The patient apparently died of syncope and heart failure. The 'asthma' might have been due to some undetermined cause, and in any case there was no clear indication for neosalvarsan injection in this particular case. The incident, however, would serve as a warning against one being guided by patients to give an injection, and using a drug of doubtful purity.—EDITOR, I. M. G.]

KNOWLEDGE OF SEX

SIR,—I have read with interest Lieut.-Colonel Owen Berkeley-Hill's paper 'A Case of Mild Hypopituitarism' published in the *Indian Medical Gazette* of March 1942, where he has stressed the sociological importance of sexual knowledge for Indians. I quite agree with the author and am surprised to find that a correspondent, writing under the caption 'Knowledge of Sex', appearing in the June 1942 number of the *Indian Medical Gazette*, has taken objection to it. His statement that the author's comments are not based on facts does not hold good, as the author's conclusions are based on the case he has cited. Unfortunately in our country, no work of a tangible



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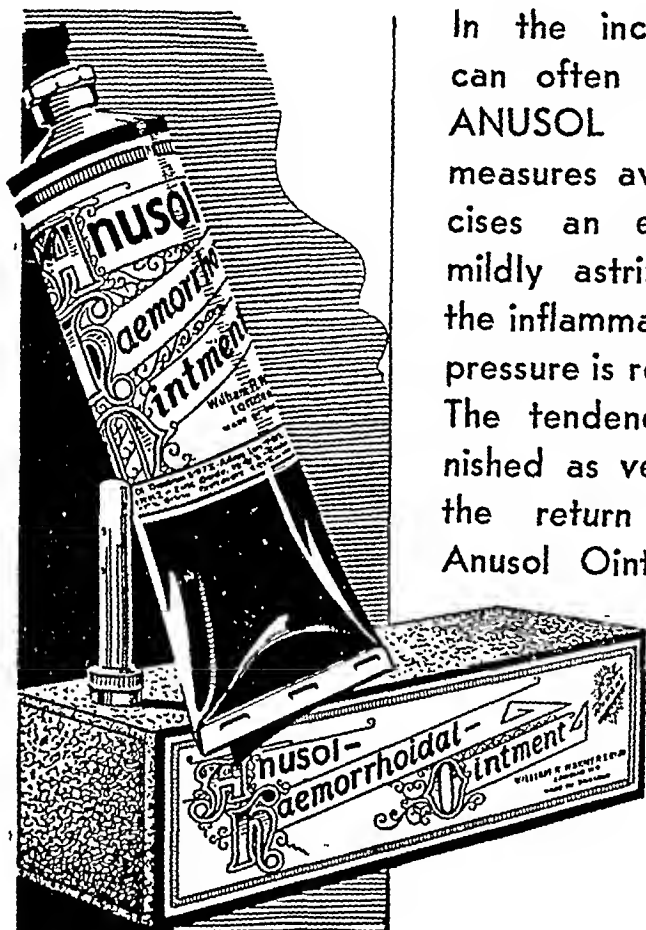
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nature has been done in this direction and so we have no reliable records to which we can refer in such circumstances. Still a few cases have come to light because of their medico-legal importance, for example two cases, where want of proper knowledge of sex has led to the death of the unfortunate wives, have been reported by Dr. Modi in his 'Medical-Jurisprudence' (page 420, Fourth Edition). The same author has reported another interesting instance of sexual ignorance in the *Patna Journal of Medicine*, Medico-Legal Supplement, January 1941, page 10. Instances of this nature can be found in plenty if a search is made for them. The fact that India's population, according to last several censuses, has shown a continuous increase, is obviously no evidence that Indians possess a proper knowledge of sex. It is high time that we realize the importance of imparting knowledge of sex to our children before they come to a marriageable age and make efforts in this direction. Bringing in the question of racial discrimination does not solve our problems and is not in keeping with our ideals of plain living and high thinking.

L. P. VARMA, M.B., B.S.

GOVIND MITRA ROAD,
PATNA,
8th January, 1943.

Service Notes

APPOINTMENTS AND TRANSFERS

THE services of Major F. R. Cawthorn, an Agency Surgeon, are temporarily placed at the disposal of His Excellency the Commander-in-Chief, with effect from the forenoon of the 26th August, 1942.

Major C. A. Bozman is appointed Officer on Special Duty in the office of the Director-General, Indian Medical Service, *vice* Colonel J. B. Hance, C.I.E., O.B.E., V.H.S., with effect from the 1st September, 1942.

INDIAN LAND FORCES

To be Lieutenants

Sharif Hasan. Dated 7th November, 1942.
Hemanta Kumar Indra. Dated 8th November, 1942.

(Emergency Commission)

To be Lieutenants

John Garden Webb. Dated 3rd April, 1942.
Stanislaus Canute Pinto. Dated 28th June, 1942.
Patrick Lawrence Karney. Dated 5th November, 1942.

Mandayam Ananthlalwar Parthasarathy. Dated 25th September, 1942.

John McDonald Dougan. Dated 14th October, 1942.

20th October, 1942

Bagh Singh Dhillon. Jagjit Singh.
Sant Singh Harnai. Yash Pal Lullah.
Muni Inder Dev Sharma.

22nd October, 1942

Hamid Shafi Qazi. Prithpal Singh.
Mohd. Mohsin Khan. Ch. Mohd. Sharif Bajwa.
Nand Kishore Khanna. Jogindar Singh Khoranna.
Zia Uddin Khan. Gautam Dev Koshal.
Ved Parkash Malhotra.

Bashir Ahmad Butta. Dated 23rd October, 1942.
Abdul Haque Khan. Dated 26th October, 1942.
Pran Nath Chhabra. Dated 29th October, 1942.
Sanadi Krishna Rao. Dated 4th November, 1942.
Miss Daphine Pacheco. Dated 3rd November, 1942.

5th November, 1942

Inam Ali Khan. Kunnumal Purail Abdul
Titti Rajagopala Seshadri. Khader.
Baji Gnaneshwar Rao. Shafiqur Rehman Khan.

6th November, 1942

Robert Francis Noronha.
Nani Mohan Bhattacharyya.
Maximilian Raskino.
Hridindra Nath Roy.

Innocent Robinson Bazziel.
Bhupendra Mohan Banerjee.
Biswa Ranjan Sen Gupta.
Mohd. Bashirul Rahman Khan.
Digambar Amrit Punolik.
Prakash Chandra.
Chandra Sekhar Prasad Sharma.
Bhola Nath Sarkar.
Animesh Chandra Basu.
Henry Demetrius Massiahdas.
Amulya Ranjan Dutt.
Nihar Ranjan Gupta.
Arun Kumar Bhattacharyya.
Bamandas Banerjee.
Niranjan Chatterjee.
Neville Anthony Durham.
Krishnajiban Majumdar.
Bishambar Nath Narula.

7th November, 1942

Bossuet Lamartine Silveira.
Ramavatar Prasad.
Narayana Iyengar Sreenivasan.

8th November, 1942

Akepati Sivarama Reddy.
Settur Sankaralinga Muthanandam.
Kartar Singh Kalra.
Mahadeva Iyer Venkateswaran.
Niranjan Choudhury. Dated 9th November, 1942.
Sesha Padmanabhan Iyer. Dated 12th November, 1942.
Laurence Eugene Chaves. Dated 10th November, 1942.
Peter Anthony Lane Roberts. Dated 26th June, 1941.
Max Berthold Klein. Dated 10th July, 1941.
John Michael Mungavin. Dated 21st February, 1942.
Jean May Drury-White. Dated 26th July, 1942.

(WITHIN INDIAN LIMITS)

To be Lieutenants

Ramesh Chandra. Dated 2nd November, 1942.
5th November, 1942

Laxmi Narayan.
Mannargudi Srinivasa Narayanan.

6th November, 1942

Praphulla Kumar Sen. Har Bhagwan Das.
Indra Narayan. Albert Jayme Rebeiro.
Mulk Raj Juneja. Ramchandra Rao Dhur-
Hussain Reza. jaty.

7th November, 1942

Kamarazu Surayanarayana Rao.
Vikhari Ekambaram.

To be Lieutenant for service in the Indian Air Force
Barun Kumar Mukherji. Dated 13th October, 1942.

(DENTAL BRANCH)

To be Lieutenants

4th September, 1942

Norman Pinto.
Man Mohan Nath Khosla.
Aum Prakash.
Arya Bhusan Marwaha.
Ramchandra Vinayak Bhagwat.
Madhukar Narayan Phadke.
Amulya Kumar Nandy. Dated 5th September, 1942.
Jai Narain Saksena. Dated 6th November, 1942.

PROMOTIONS

Majors to be Lieutenant-Colonels

W. D. B. Read. Dated 16th November, 1942.
E. G. Hurd-Wood. Dated 30th November, 1942.
T. J. Davidson. Dated 6th December, 1942.
G. S. Gill. Dated 20th December, 1942.

LAND FORCES

(Emergency Commissions)

Lieutenants to be Captains

7th July, 1942

H. M. Garlick. M. Scott.
J. S. Laurie. M. Lawton.
D. G. Coutts. E. M. Eldrid.
A. A. M. Coutts.

T. E. W. R. Wood. Dated 10th July, 1942.
J. W. Lusk. Dated 7th October, 1942.
C. H. Merry. Dated 23rd October, 1942.

*Lieutenants (on probation) to be Captains
(on probation)*

C. H. Phillips. Dated 3rd July, 1942.
E. R. James. Dated 10th August, 1942.
E. N. Pearlman. Dated 26th August, 1942.
A. B. Rustom. Dated 12th August, 1942.
S. R. Kidiyoor. Dated 4th September, 1942.
O. K. T. Kesavan. Dated 5th September, 1942.
B. S. Row. Dated 7th September, 1942.
R. Natarajan. Dated 9th September, 1942.

2nd October, 1942

K. M. Fozdar. B. N. Roy.
J. V. Nazareth. R. D. Marathe.
V. N. Ambalavanan. Dated 2nd October, 1942.
A. Sitarammurti. Dated 5th October, 1942.
M. M. Deshpande. Dated 6th October, 1942.
(Miss) C. Shepherd. Dated 2nd September, 1942.
S. K. B. Ray. Dated 1st September, 1942.
Jalal-Ud-Din. Dated 25th September, 1942.
A. K. Chatterjee. Dated 30th September, 1942.

25th October, 1942

A. B. Rau. M. S. K. Murthy.
P. S. Rao. T. Devairakkam.
P. R. C. Reddy. J. E. Abraham.
M. Ikram. A. Balasubramanian.
S. Z. Ahmed. S. N. Ganapati.
A. R. Natarajan. S. Ranganathan.
P. S. Menon. S. R. Rao.
P. Krishnamurthy. V. C. Venkatachalam.
C. Balakrishnan. C. N. J. Aiyannadar.
J. S. Scerma. A. M. Seshan.
G. H. Durairaj. K. M. K. Mohammad.
S. I. Gopalakrishnan. A. A. Appadorai.
A. K. Haridass. K. T. R. Nair.
P. V. Ramachandran. N. D. Ramaswami.
C. K. Ramchandrar. J. R. K. Rao.
S. R. Sarvothaman. C. R. Chandrasekhar.

11th May, 1942

K. N. Sastri. K. Suryanarayana.
B. R. Karnad.

(Mrs.) G. Connor. Dated 1st August, 1942.
(Miss) P. D. Nanavatty. Dated 21st August, 1942.
(Miss) G. K. Dhariwal. Dated 29th August, 1942.
M. A. Parthasarathy. Dated 25th September, 1942.
M. M. A. Dubash. Dated 28th September, 1942.
M. Krishnamurthy. Dated 1st October, 1942.
H. K. Indra. Dated 8th November, 1942.

5th September, 1942

S. S. Hazra. C. E. Varkkey.
S. N. Ray. S. C. Roy.
B. K. Gupta.
V. V. Pradhan. Dated 6th September, 1942.

7th September, 1942

V. C. Kamaraju. K. N. Raman.

*Lieutenants (on probation) to be Captains
(on probation)*

(Mrs.) R. K. Puri. Dated 1st August, 1942.
K. S. Rau. Dated 7th August, 1942.
(Miss) A. M. Waters. Dated 18th August, 1942.
(Miss) S. M. Rapson. Dated 19th August, 1942.
(Miss) P. B. Bellhart. Dated 21st August, 1942.
(Miss) B. M. Burgess. Dated 24th August, 1942.
(Miss) E. Mitra. Dated 29th August, 1942.
B. Lall. Dated 4th September, 1942.
(Miss) B. Natarajan. Dated 14th September, 1942.
E. Dikshitulu. Dated 21st September, 1942.
E. K. P. Nambiar. Dated 24th September, 1942.
E. C. Srinivasan. Dated 28th September, 1942.
O. P. Markandya. Dated 10th December, 1942.
(Miss) E. H. Smith. Dated 22nd September, 1942.

(WITHIN INDIAN LIMITS)

Lieutenant to be Captain

S. S. Chhabra. Dated 9th October, 1942.

*Lieutenants (on probation) to be Captains
(on probation)*

7th August, 1942

S. R. Row. N. N. Singh.
A. S. Sen Gupta.
N. G. Rajulu. Dated 8th August, 1942.
S. V. Krishnayya. Dated 9th August, 1942.
B. D. Mistry. Dated 15th August, 1942.

4th September, 1942

C. A. Rodrigues. A. C. Sood.
T. A. A. Ananthakrishnan. W. J. C. Rebello.

ARMY IN INDIA RESERVE OF OFFICERS (MEDL.)

Captains to be Majors

24th October, 1942

L. S. Anand. D. N. Basu.
K. C. Virmani. D. C. Datta.
P. N. Sathe. S. K. Ganguli.
A. N. Narang.

RETIREMENT

Major J. H. Boulbee, on account of ill health.
Dated 26th September, 1942.

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Original Articles

CLINICAL EXPERIENCES OF VITAMIN DEFICIENCIES IN MYSORE*

By ROBERT HEILIG, M.D.

(From Krishnarajendra Hospital and Medical College, University of Mysore)

It is possible that in the U.S.A. vitamin deficiencies are diagnosed too frequently due to the deep impression created upon the mind of physicians by the brilliant successes in the experimental production and cure of various syndromes following withdrawal or supply of single vitamins or vitamin complexes in animals. This at least is the opinion expressed in the last volume of the Mayo Clinic publications (1941) where Butt quotes that in 1938 the U.S.A. spent 54,000,000 dollars on vitamin preparations. It is probable also that the warning against missing pathological conditions requiring anything but vitamins is justified in the West. Here, in India, certainly the opposite mistake is committed much more frequently; at least outside the big cities and research centres, nutritional deficiencies are far too rarely recognized as such, and still more rarely is the deficient factor or group of factors properly determined. A deficiency map of India should be worked out so that the medical man and health officer working in a certain region could determine exactly which clinical deficiency syndromes are to be expected in his area and how they could be remedied. Much important work has been done towards achieving this aim. Apart from McCarrison's pioneer work, numerous very valuable investigations on nutrition and deficiency diseases were carried out by Aykroyd, Krishnan and co-workers in South India including Travancore and the Nilgiris since 1936; in Coorg by Bhave and Bopaiya (1942); in Orissa by Singh (1939); by Wilson, Ahmad, and Mullick (1936), Wilson, Ahmad and Mitra (1937), Wilson and Mitra (1938), and Ahmad and Mullick (1940), in Calcutta, North Bengal and Assam; by Mitra (1940-41) in Jamshedpur, among aboriginal tribes in Bihar and coal miners in Jharia; by Bhave (1941) in C. P. and Berar; by Shourie (1939) in Delhi Province; Ahmad and Gore (1938) in the Punjab; and, finally, as 'a comparative nutritional survey among various Indian communities' by Wilson and Widdowson (1942), preceded by a research on diet and nutrition in North India by Wilson, Widdowson and Wait (1937), Wilson's investigations of osteomalacia and rickets and her reports on deficiency diseases in Kashmir (1939). Still more field work has to be carried out ere our knowledge of the nature and extent of avitaminoses

all over India can be called satisfactory. However, taking the broad average of all these investigations, one seems to be justified in saying that India suffers from A- and B-complex deficiency as far as vitamins proper are concerned, and from a considerable lack of animal protein, calcium, and, to a smaller extent, fat; whereas C-deficiency becomes prominent only in definite famine-areas (Khan, 1942), and an insufficient D-supply, independent of economic conditions, is manifest everywhere where the purdah system is in force. It is interesting to compare the nutritional conditions in India with those in N. China where the main deficiencies are in A, C and D, whereas the B-vitamins are represented satisfactorily, thanks to the use of millets as staple food; where even more than here, there is generally, a very serious insufficiency of calcium intake (Snapper, 1941). Regarding the conditions in Mysore we do not intend to present complete statistics but only to report on clinical experiences derived from hospital practice.

As far as ophthalmic conditions are concerned I am indebted to Dr. A. M. Ponnambalam* and Drs. S. Vasudeva Rao and Sundar Rao† for furnishing me with a summary of their findings. All the data related to deficiency conditions in pregnancy are derived from the experience of Dr. Miss K. S. Captain.‡

Vitamin A.—The assessment of A-deficiency on the basis of the frequency of follicular keratosis or phrynodema among children and young adults, was shown to be unreliable by Aykroyd and Rajagopal (1936) and Aykroyd and Krishnan (1937) who found that this skin condition does not appear in any strict connection with A-supply; Wilson and Widdowson (*loc. cit.*) point out its dependence upon female seclusion in N. India. It is certainly not safe to use the incidence of phrynodema as an indication of A-deficiency. Another method of estimating a moderate lack of A-supply is the observation of conjunctival pigmentation and Bitot's spots; but Kirwan, Sen and Biswas (1941) found that 88 per cent of patients showing these signs have a normal dark adaptation which certainly is a more reliable clinical method for estimating the A-balance; recent work shows night-blindness to be a late manifestation of A-deficiency, following weeks of a low A-blood level (Brenner *et al.*, 1942), due to the fact that the retina retains its vitamin A-stores longer than the liver and the blood (Lewis *et al.*, 1942). Therefore, we used only the presence of night-blindness, xerosis and keratomalacia as indicating a definite A-deficit.

The table shows the absolute and relative frequency of these three conditions in Calcutta, Bangalore and Mysore.

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TABLE

Place	Number of ophthalmic patients	Period of investigation	A-DEFICIENCY DISEASES					Authors
			Total Number	Per-centage	Night-blindness %	Xerosis %	Kerato-mal. %	
Calcutta ..	14,698	4 months	386 *	2.6	10.6	77.2	12.2	Kirwan <i>et al.</i> , 1941.
Bangalore ..	63,100	2 years	818	1.3	13.8	68.5	17.7	Ponnambalam, 1941-42.
Mysore ..	11,000	1 year	220	2.0	12.0	84.0	4.0	Vasudeva Rao <i>et al.</i> , 1942.

* Groups III and VI (33 cases) of the Calcutta workers were excluded from this comparative survey because neither of the conditions forming them, *viz*, diminished sensibility of the cornea and phthisis bulbi, has been included in the figures from Bangalore or Mysore.

In Mysore the majority of night-blindness cases came from the rural areas. Xerosis more frequently was seen among boys, especially of secondary- and high-school age, than among girls. In Mysore 75 per cent (in Calcutta 72 per cent) of keratomalacia was found in children up to the age of five years; the remaining two cases were women after delivery. In Bangalore 32 grave cases of keratomalacia post-partum were seen during the last five years. The surprisingly low percentage of this condition in Mysore, *viz*, 4 per cent against 12.2 in Calcutta and 17.7 in Bangalore, is in agreement with the fact that during the last two years no case of keratomalacia has occurred in the Maternity Hospital, Mysore, whereas in previous years such patients were fairly frequently seen there. Whether this fact is due to the improved and extended local maternity welfare work will be decided by future experience.

During the same period two cases of keratomalacia were observed in the medical wards in women suffering from protracted diarrhoea, which certainly aggravated the consequences of a low vitamin-A intake.

Night-blindness and xerophthalmia respond well to cod-liver oil which in the latter cases was also used by external application. Keratomalacia practically always leads to phthisis bulbi, being still the cause of many cases of preventable blindness. For working out a vegetarian diet which is sufficiently rich in vitamin A one has to keep in mind that among all the reddish-yellow pigments present in vegetables and fruits, only beta-carotene serves as the pro-vitamin A, and that only a fraction of vegetable carotene is transformed into vitamin A; whereas practically all the A present in cod-liver oil is absorbed by rats, only 21 per cent of the carotene of alfalfa leaves appear as vitamin in the liver stores (Treichler *et al.*, 1942). Therefore, it is very fortunate that the Indian shark- and sawfish-liver oils are such very rich sources of vitamin A (Majumdar, 1941), though it would be desirable to increase their D-content by fortifying them with calciferol (Ranganathan, 1941). Further, it is important to remember how many different factors are apt to counteract or to destroy this vitamin. It is easily oxidizable, sunlight completely destroys it in thirty minutes (Muthanna and Seshan, 1941) and on a low level of intake its action is neutralized by unsaturated fatty acids such as methyl linolate and linolenate (Sherman, 1941). This fact most probably explains the observation that the inclusion of coconut cake in the diet interferes with A-utilization (Ramasarma, 1942).

Vitamin B₁.—It is a surprising fact, confirmed by all the clinicians working in this part of the country, that a clear-cut B₁-deficiency under the picture of beri-beri is not encountered among our patients. This experience is partly due to the fact that in some districts of Mysore State, such as Kolar, ragi (*Eleusine coracana*), and in others, cholam (*Sorghum vulgare*) form the staple food, and parboiled rice is mostly used by people coming from Madras Presidency or the West Coast. Nevertheless a considerable part of the population, especially the poorest among the town dwellers, does live mainly on polished rice, but without developing beri-beri. This is certainly explained by the regular consumption of some pulses—dhal, gram, etc.

Nevertheless some symptoms of aneurin-deficiency are found frequently enough; subjective sensations of pins and needles, numbness, called by our patients 'djum djum', up to real neuralgic pains in the calves and toes, much rarer in the upper extremities and fingers, constitute complaints in well over one-third of our female and about 20 per cent of male patients. They are still more frequent in pregnancy. Real neuritis of the sciatic nerve and the brachial plexus is rarely seen and is mostly of syphilitic or diabetic origin, though the severest case of a sciatica, seen in an elderly medical practitioner, responded only to thiamin-injections. Having established by therapeutic tests with thiamine hydrochloride that the paræsthesias and neuralgias in the majority of our cases are due to an insufficient B₁-intake, our routine treatment consists of giving rice-polishings, five teaspoonsful a day, mixed with buttermilk or lime juice.

A syndrome which probably belongs to the same group is chest pain of long duration in otherwise healthy young to middle-aged individuals; it is much more common among men, especially hostel students; though neurotic factors certainly are involved in some of these cases, rice-polishings seem to improve the condition. Some of these patients whom we followed up for more than two years and who did not respond to antineuralgic and antimalarial treatment to diathermy, shortwaves, strapping, intradermal injections of plenocaine, etc., lost the pain completely when marmite was used regularly; when this yeast preparation disappeared from the market, they returned with the same complaint and responded either to rice-polishings or, still better, to dry yeast, though no sign of any other B-factor deficiency was present. A systematic

investigation of this question with which we are confronted every day is planned.

An interesting manifestation of thiamin deficiency was seen in our eye-department. Two women, about 35 years old, showed a unilateral external rectus paralysis. All the investigations giving negative results, a course of berin injections was tried and cured the condition in both these cases in a couple of weeks.

An important syndrome was described and shown to me by Dr. Captain. Towards the end of pregnancy or soon after delivery in very anæmic women, a stomatitis develops, consisting first of white opaque spots of millet grain size on the mucous membrane of lips and cheeks, accompanied by an unbearably foul smell and leading in all untreated cases to ulceration which reminds one of a beginning cancrum oris. Early cases respond to thiamin injections; as soon as ulcer formation sets in, the prognosis is extremely grave. No detailed blood examinations have been performed, but clinically these cases remind one of aplastic anæmia which—according to these experiences—should be given a trial with B_1 therapy.

B_2 -complex.—Of more frequent occurrence in our clinical material is a syndrome due to the deficiency of certain members of the B_2 -complex.

Throughout the year a high percentage of our hospital beds are occupied by cases of chronic diarrhoeas of a few weeks' to two years' duration. The majority of them are observed in young and middle-aged women. After excluding true dysenteries a well-defined group remains which is characterized by a moderate glossitis with a few red patches on the tongue in acute cases, leading to slate coloured pigmentations and in late stages to a widespread epithelial atrophy; subjective symptoms include a burning sensation on taking spiced food. Loose motions are passed five to eight times a day which for several weeks show all the signs of an enteritis; they are not watery but of the consistence of a thin congee and have a bright greenish-yellow colour, reminding one of jejunal bilirubin diarrhoeas; their reaction varies and they do not contain any substantial amount of mucus. Microscopically ill-digested starch granules which give a faint pinkish iodine reaction, nucleated epithelial cells and a few leucocytes are present. Fat is absent. In cases of long standing, symptoms of colitis become prominent; the colour of the motions is darker; mucus or even mucus appears in lumps, frequently separated from the stool; epithelial nuclei are absent and leucocytes present in fair amount. Equally different is the radiological picture in these two stages. As long as the character of a simple enteritis is maintained, the stomach empties the barium meal speedily in the beginning, according to the hypo- or achlorhydria which always is found; but, after six hours, a varying amount of barium is still visible in the stomach; the motility of the small intestines is usually markedly increased; in many cases the head of the meal reaches the cæcum in less than one hour; the mucosal pattern of the small intestine seems to be coarser than normal, whereas the colon shows normal conditions. In the later stage the examination by barium enema shows all degrees of colitis, from mere spasticity to irregular haustration and granular hypertrophy up to a fully developed pipe-stem appearance of the descending colon, due to complete atrophy of the submucosal nerve-plexus. A hypochromic anæmia belongs to the picture, increasing with the duration. None of these cases showed any typical signs of pellagra, such as skin lesions or mental derangement, and none had fatty motions of a sprue-like character. Nevertheless many of them respond surprisingly quickly to injections of nicotinic acid, though they are refractory to our routine treatment, by which practically all the other diarrhoeas are benefited.

To define this group of nicotinic acid deficiency as distinctly as possible, excluding spontaneous or chance improvements, initially all

cases of diarrhoea which did not show any macro- or microscopic signs of any kind of dysentery were put on a diet consisting only of grated apple or mashed plantain pulp, well stirred up in a tepid weak tea infusion without sugar or milk; if this regime, effective in many unspecific diarrhoeas, did not control the motions within 48 hours, bismuth and carbo-caolin or ultrindon in full doses were added to it and whole wheat 'conjee' was included in the diet. In those cases still showing no improvement, a course of enterovioform or carbanthren was given two to three days later. Only the remaining group of persisting diarrhoeas was treated with nicotinic acid on a diet consisting of wheat 'conjee'. After five nicotinic acid injections of 50 mg. each, in almost all of these cases one or two well-formed or thick pasty motions are passed a day, and in many of them the general condition, appetite and red blood count improve quickly. Having had experiences of this kind for about two years, we now start the treatment at once with nicotinic acid in all patients with non-dysenteric diarrhoea, who show any signs of an acute or chronic glossitis. It may be mentioned that the angular stomatitis of ariboflavinosis does not belong to this picture.

Though nicotinic acid rectifies the bowel action in these cases, in some of them it is necessary to add crude liver extract not so much for the sake of blood regeneration but because sometimes the radiological appearance of the small or large intestines remains pathological, or because of persistent œdema which developed due to the severe hypoproteinæmia. Though thiamin is of no avail, crude liver extract is very effective. Liver is superior to nicotinic acid for at least two reasons. It supplies riboflavin which acts as the co-enzyme factor required for re-oxidizing the reduced co-enzymes I and II, the main factor of them being nicotinamide; thus, for maintaining the nicotinic acid activity, riboflavin is needed. Moreover, liver may be a better source of B_1 than the small doses of thiamin available, and in our cases B_1 might be necessary for restoring the damaged submucosal nerve plexuses, and for restoring the tone of the autonomous nervous system. In the absence of B_1 -pyrophosphate, the co-carboxylase, pyruvic acid accumulates and prevents the oxidation of lactic acid; both of them interfere with the nervous functions responsible for normal intestinal motility and haustration. But B_1 is required also for the hydrolytic breaking up of choline, cholinesterase being inactive in the absence of B_1 (Bernheim, 1940). The choline accumulation resulting from vitamin B_1 deficiency causes para-sympathetic stimulation which causes intestinal hypermotility. Lucid accounts of this functional interdependence of thiamin, nicotinic acid, and riboflavin were given by Datta (1941), Giri (1942) and Swaminathan (1942a).

For correlating our syndrome with experiences recently described elsewhere, it may be mentioned that Golden (1941) and Mackie (1941)

described a syndrome in man, characterized by anorexia, a radiological 'deficiency pattern' of the small intestines, and a flat oral glucose tolerance curve; these symptoms are recognized as manifestations of B-complex deficiency and respond better to crude liver extract or yeast than to any single B-factor.

Manson-Bahr (1941) found nicotinic acid and liver extract effective in a condition of stomatitis accompanied by some bowel derangement, the character of which, together with a macrocytic anæmia, reminds one of sprue. Rao (1942) put monkeys on a 'poor South Indian diet', consisting mainly of milled rice. Many of these animals developed a glossitis and diarrhoea. Histologically they showed a considerable epithelial degeneration and mucosal atrophy in the lower ileum.

The fully developed picture of pellagra is not seen here but pellagroid skin conditions, such as symmetric thickening, coarseness, scaliness on cheeks, forearms and wrists accompanied by some glaziness of the tongue and a history of a tendency to loose motions, occur occasionally. The skin lesions respond to nicotinic acid. Quite recently we treated two men of 25 to 30 years of age, showing clouded consciousness, cogwheel rigidity and severe anorexia, with intravenous injections of nicotinic acid (50 mg. per day); the condition of one of them considerably improved, conforming with the results of Cleckly and Jolliffe (Butt, *loc. cit.*); the other one remained uninfluenced.

Among the signs of ariboflavinosis, only angular stomatitis is observed; no magenta-coloured and rarely a fissured tongue, no cheilosis and especially no superficial keratitis (Aykroyd and Verma, 1942) are encountered. Angular stomatitis being seen here only in women, an accompanying scaly dermatitis of the scrotum was not observed. Dried yeast in doses of 2 teaspoonsful a day cures this condition in a few days. An important manifestation of B-complex deficiency is nutritional or tropical anæmia, mostly seen in pregnancy, our other anæmia material consists almost exclusively of iron-deficient anæmias. About 70 per cent of the cases in the maternity hospital are found to require liver. The fact that only crude liver extracts are effective makes it probable that the B-complex is the active principle.

Vitamin C.—Definite manifestations of C-deficiency are rarely seen in our medical wards. We find every year about half a dozen of cases with swollen spongy gums, some hardly able to chew their food because of the severe gingivitis which often causes considerable oozing of blood. All of these patients confessed to not taking any green leafy vegetables—unless they are cooked for hours—and to dislike any kind of raw fruit. They respond within a few days to full doses of vitamin C such as injections of 'redoxon forte'. Smaller doses are usually useless. To prevent a relapse in these cases, we recommend the regular consumption of *phyllanthus emblica*,

called here 'nellikai', which according to Giri (1939) and the Coonoor-workers is by far the best natural source of ascorbic acid. That at least a part of our female population lives on the borderline of C-deficiency is shown by the fact that severe gingivitis with purulent discharge is seen much more often in pregnant women who definitely state that this condition appears whenever they are pregnant and subsides after delivery. Such a latent lack of vitamin C was found by Basu and Ray (1940) in a small group of Bengali boys, but not among 120 medical students in Madras, examined by Sitaramurti (1942).

Infantile scurvy, Moeller-Barlow disease, is seen here about twice a year with typical radiological findings and prompt response to ascorbic acid.

Vitamin D.—Just as A-deficiency is mostly seen by the ophthalmologist, D-deficiency, manifested as osteomalacia, occurs predominantly in the maternity wards. There mild cases are found quite frequently among both Hindu and Mohammedan multiparas; the incidence and severity definitely increase proportionately with the number of deliveries, which means that calcium and vitamin D stores are progressively depleted by every additional period of pregnancy and lactation. In first or second pregnancies severe cases of osteomalacia which make a caesarean section necessary are almost confined to purdah-ladies; an interesting and unexplained exception to this rule is found in women of the Comtee caste, well-to-do people who do not practise the purdah system and are non-vegetarians. A similar observation was made by Green-Armytage (1928) among wealthy Marwari women in Calcutta. Among non-pregnant women, osteomalacia of a higher degree is practically confined to Mohammedans, just as rickets, of which every year about six to eight florid cases are admitted, is far more common among purdah-children. Among ophthalmic patients during the last year, three cases of lamellar cataract were seen, which is supposed to be due to a lack of vitamin D.

Though definite D-deficiency diseases are in a low percentage among our medical patients, latent tetany, characterized by a highly positive Chvostek's sign, is very frequent among them, especially in girls and young women but by no means confined to them. This common occurrence of tetany, in spite of the abundance of ultraviolet rays and a sufficient exposure of the skin to them, is due to the extremely low intake of utilizable calcium. The milk consumption being negligible, the only calcium sources are cereals and leafy vegetables. Due to the high phosphorus content of the cereals, their calcium is present either in the form of phytin or as a calcium salt of phytic acid; neither of them can be absorbed (Harrison and Mellanby, 1939). Green leaves are rich in oxalic acid which renders the calcium insoluble, and thus almost useless (Rau and Murty, 1942); whereas 87 per cent

of milk calcium is utilized (Fincke, 1941), only 13.4 per cent of the calcium present in carrots is utilizable (Breiter *et al.*, 1942). Moreover, phytic and oxalic acids even precipitate calcium present in other foodstuffs such as milk, still further increasing the calcium deficit; these losses make a considerable D-supply imperative for preventing the development of serious deficiencies.

It may be mentioned that vitamin E as wheat germ oil is the routine medication of habitual abortion in the Maternity Hospital (Mysore) and that their highly beneficial effects are observed in spite of the sceptical reports in recent, especially American, literature.

We have no experience with the very interesting vitamin H or biotin.

Vitamin K is used in our surgical wards for the control or prevention of hæmorrhages in jaundiced patients.

Conclusions

At the first glance, malnutrition is not the most urgent health problem in Mysore State; hookworm disease and, in a good many districts, malaria form much more formidable threats to the population. This impression is confirmed by the experiences of Dr. Chendrashekariah who collected data of the usual food intake at the Health Centre in Closepet, and handed them to B. G. Kirshnan for analysis. Though, as far as we know, not worked out in detail this material did not show any serious deficiency. And yet our people are definitely living on the borderline of numerous deficiencies which at once become manifest when an additional strain is put upon their system. The highest degrees of hookworm anæmia existing anywhere are of frequent occurrence in Mysore. American mass investigations make it probable that hookworm infestation causes severe anæmia only in B-complex deficiency. Severe cases of malarial cachexia just compatible with life are admitted every day. Many cases of unresolved pneumonia and of lung abscess are continuously under our treatment, proving an inability of normal enzyme production. At times as many as 30 per cent of our in-patients show koilonychia, brittle, spoon-shaped nails due to iron deficiency. These facts show how necessary it is to increase the general resistance of our people. That is not merely a question of income; in Jamshedpur, for example, Mitra (1940a) found the C-intake higher among the poorer classes, and Wilson and Widdowson (*loc. cit.*) emphasize that because of ignorance and conservatism even present resources are not fully utilized. It is a question of teaching the people, in village and town alike, how to build up a better health standard by eating the right kind of food. Green leaves and papaya, parboiled*

unpolished rice or ragi, nellikai, the Indian gosseberry, and even some kind of citrous fruits are available for everybody, and so is sunlight. A special problem is that of a sufficient milk supply to everybody, especially to pregnant and lactating women and children. But here again our population has to be persuaded to make an effort towards this end, to overcome their dislike to milk (Shivaram, 1942). At present, the vast majority of our hospital steadily refuse to take milk or any kind of milk products because, in their opinion, buttermilk and curds cause cold and swelling all over the body, whereas "Sāru", vegetable cooked to death, is their ideal food.

We intend to form health squads consisting of our medical students for starting and maintaining a 'happiness through health' campaign among our people. Under the guidance of our Medical College they should collect facts pertaining to nutritional and general health conditions, and at the same time spread some knowledge of better sanitation and healthier food habits, which is so badly needed for the sake of transforming preventable diseases into prevented diseases.

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*The many advantages of parboiled over any other kind of rice have been investigated and the great practical importance of parboiling for mass nutrition was established by Aykroyd (1932), Aykroyd *et al.* (1940) and Swaminathan (1941, 1942).

A CASE OF CONTINUED FEVER DUE TO *SALMONELLA (BACTERIUM) ENTERITIDIS* (GAERTNER)

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and

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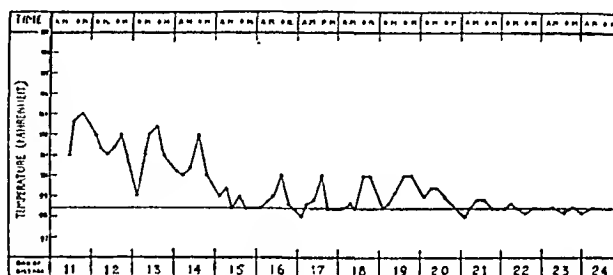
Bact. enteritidis usually gives rise to symptoms of food poisoning in man, but there are records of this organism causing other diseases. Smith and Scott (1930), for example, describe three cases of continued fever in which the 'Dublin' type was isolated from the blood. Guthrie and Montgomery (1939) reported a series of cases, most of which had occurred in the form of small epidemics among infants, with severe catarrhal enteritis, septicaemia, meningitis and purulent cholecystitis. As there are not many such cases on record in literature, the following case, in which *Bact. enteritidis* was recovered in pure culture from the blood during the routine bacteriological examination for enteric infections in

the wards of the Mayo Hospital, may be of some interest:—

Clinical features

Patient Gopi Chand, aged 5, Hindu male child (Burma evacuee), was admitted into the Mayo Hospital on 2nd July, 1942, on the 11th day of his illness with continued fever. On his way to India he had fever for a few days, of unknown nature. The fever subsided and the temperature remained normal for about six days but again started to rise and the patient was admitted into a hospital at Calcutta; he was discharged after 10 days. After remaining afebrile for about a fortnight he started having fever again and was admitted into the Mayo Hospital, Lahore, on the 10th day of the present illness and was discharged on the 24th day. He had continued remittent fever of enteric type (see chart).

CHART



The spleen was enlarged two fingers below the costal margin and firm. The liver was slightly enlarged. He was passing two to three motions a day. There was slight distension of the abdomen, which lasted for a few days.

Bacteriological findings

Technique.—Five c.cm. of blood were taken on the 3rd day after admission (13th day of fever) and inoculated in 10 c.cm. of ox bile. After 24 hours' incubation, subcultures were made on an agar slope, and in four carbohydrate media, viz, lactose, glucose, mannite and saccharose. Examination of these cultures showed that the organism was a non-lactose fermenting, Gram negative, motile bacillus which fermented glucose and mannite with gas production, considered possibly to be one of the paratyphoid group. Slide agglutination tests were carried out with para A and para B sera, but results were negative. The reaction was however positive with typhoid 'O' serum. A more detailed examination of the organism was then carried out and the results are given below.

Biological characters.—The organism was grown in peptone water containing various carbohydrates. It produced acid and gas in glucose, mannite, maltose, dulcitol, rhamnose and arabinose. It did not ferment lactose and saccharose. It did not form indol.

It will be noted that the strain under investigation promptly fermented both arabinose and rhamnose. The 'Dublin' type either does not ferment arabinose or does so slowly. This cultural distinction serves to distinguish the *Bact. enteritidis*, 'Dublin', from *Bact. enteritidis*. Besides these usual carbohydrate reactions there are three other tests, which have been extensively used in the identification of the members of the

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Salmonella group, namely, Bitter's medium (see Smith and Scott), Stern's glycerol solution, and decomposition of d-tartrate (Topley and Wilson, 1936). In our study of this strain we have made a comparison with one stock strain of *Bact. enteritidis* and one of 'Dublin' type. The results of these investigations are shown in table I. From the study of the table it will appear that the reactions of this strain are identical with those of the stock *Bact. enteritidis* with the exception of slow fermentation (48 hours) of arabinose in Bitter's medium. In this connection we may refer to the opinion of Kuffmann and others (quoted by Guthrie and Montgomery), who have had a considerable experience of Salmonella strains, that these tests are not very reliable owing to variability in cultural reactions.

Serological characters.—The culture of the organism was agglutinated by *Bact. typhosum* 'O' antiserum but not by the para A or para B 'O' and typhoid 'H' antisera. Antityphoid 'O' serum reacts with the somatic antigen (IX) which *Bact. typhosum* shares with the various types of *Bact. enteritidis*. In order to differentiate the various members of group D possessing a common IX somatic antigen, it was necessary to carry out agglutination and absorption tests, the results of which are set out in tables II and III. The results of the agglutination and absorption tests with 'O' antisera which are detailed in table II show that the X organism under investigation is not agglutinated by paratyphoid 'O' sera at all, but that it reacts to the full titre with typhoid 'O' serum and with *Bact. enteritidis* serum. Absorption of these sera with thick suspensions of the X organism leaves the agglutinins for para A, B, and C intact, but removes all the agglutinins for *Bact. typhosum* 'O', *Bact. enteritidis* of the 'Dublin' type. Thus it can be concluded that the 'X' organism belongs to group D of the Kuffmann-White schema. This group is composed of several varieties of *Bact. enteritidis* and other organisms which all contain the same 'O' antigen, namely, IX.

TABLE I

Results of special fermentation reactions

Organism	BITTER'S MEDIUM		Fermentation of d-tartrate
	Arabinose	Rhamnose	
<i>B. enteritidis</i> (stock strain).	+	+	+
<i>B. enteritidis</i> var. <i>Dublin</i> (stock strain).	—	—	—
Organism X	±	+	+

Explanation : ± = late fermentation.
+ = fermentation.

Further differentiation within this group can only be carried out by agglutination and absorption tests with 'H' sera containing the specific

TABLE II

Agglutination and absorption tests with 'O' antisera

'O' antisera	UNABSORBED ANTISERUM		ANTISERUM ABSORBED WITH X 'O' ORGANISM	
	Agglutinates organism—	Titre	Agglutinates organism—	Titre
<i>B. paratyphosum</i> A.	<i>B. para</i> A 'O' X 'O'	250 25	<i>B. para</i> A 'O' X 'O'	250 nil
<i>B. paratyphosum</i> B.	<i>B. para</i> B 'O' X 'O'	250 nil	<i>B. para</i> B 'O' X 'O'	250 nil
<i>B. paratyphosum</i> C.	<i>B. para</i> C 'O' X 'O'	250 nil	<i>B. para</i> C 'O' X 'O'	250 nil
<i>B. typhosum</i>	<i>B. typhosum</i> X 'O'	250 250	<i>B. typhosum</i> X 'O'	nil nil
<i>B. enteritidis</i> 'Dublin'	'Dublin' 'O' X 'O'	250 250	'Dublin' 'O' X 'O'	nil nil

Explanation : X = Organism under investigation.

'H' antigens. Table II shows the effects produced on a suspension of the X organism and related organisms by these different antisera, namely, *Bact. enteritidis* (g, o, m), *Bact. enteritidis* var. 'Dublin' (g, p), *Bact. enteritidis* var. *Moscow* (g, o, q), *Bact. enteritidis* var. *Rostock* (g, p, u).

TABLE III

Agglutination and absorption experiments with 'H' antisera

'H' antisera	UNABSORBED ANTISERUM		ANTISERUM ABSORBED WITH X 'O' ORGANISM	
	Agglutinates organism—	Titre	Agglutinates organism—	Titre
<i>B. enteritidis</i>	<i>B. enteritidis</i> X	250 400	<i>B. enteritidis</i> X	nil nil
<i>B. enteritidis</i> 'Rostock'.	<i>Rostock</i> X	250 250	<i>Rostock</i> X	250 nil
<i>B. enteritidis</i> 'Moscow'.	<i>Moscow</i> X	250 250	<i>Moscow</i> X	250 nil
<i>B. enteritidis</i> 'Dublin'.	<i>Dublin</i> X	250 50	<i>Dublin</i> X	250 nil

Explanation : X = Organism under investigation.

All the sera agglutinate the 'X' organism because they contain the agglutinins for the common 'H' antigen, namely, g. In order to establish the identity of the 'X' organism with one of these, absorption tests were carried out and results are shown in the same table III. It will be seen that when *Bact. enteritidis* serum is

absorbed with the X organism, there is complete removal of all the agglutinins for itself and for the *Bact. enteritidis*. This organism was, however, unable to absorb all the agglutinins from Rostock, Moscow and Dublin sera. These results establish the identity of the organisms with *Bact. enteritidis*. These results taken in conjunction with those of biochemical reactions show that the organism isolated from the case reported here is *Bact. enteritidis* and not *Bact. enteritidis* var. *Dublin*.

Discussion

Bact. enteritidis (Gaertner) was originally isolated by Gaertner in 1886 from a case of food poisoning, and since then by many others from similar cases. As it is met with frequently in outbreaks of food poisoning from contaminated meat, infections with this organism are uncommon in infants and young children. In adults it is not very invasive, that is to say, it has no tendency to cause septicæmia, and the symptoms are mainly those of food poisoning. On the other hand, there have been a number of instances recorded in which infants infected with this organism have shown symptoms of septicæmia, meningitis, etc. (quoted by Guthrie and Montgomery). As the identification of the causal organism in these reports was done before all the main variants, notably Dublin, had been differentiated, it seems probable that *Bact. enteritidis* was not responsible for all these cases. A recent report by Guthrie and Montgomery (*loc. cit.*) is, however, of special interest in this connection, as it takes note of all the known variants of *Bact. enteritidis*. They describe 16 fatal cases in which there was clinical evidence of blood spread. Fifteen of these were due to *Bact. enteritidis* and one only to the Dublin variety. The high mortality rate with the remarkably widespread lesions recorded by these workers illustrates the extraordinary invasive power which these organisms can assume in children. Our case of a child from whose blood *Bact. enteritidis* was isolated lends support to this view, and is of further interest in that it gave rise to continued fever of the enteric type. That *Bact. enteritidis* (Gaertner) may cause continued fever in man has been known for a long time, but, as the identification of the organism recovered from these cases was carried out before the discovery of several of the variants, it has been suggested that most of the earlier cases were probably due to *Bact. enteritidis* var. *Dublin* and not to *Bact. enteritidis*. This view is supported by Smith and Scott (*loc. cit.*) who isolated the 'Dublin' type from the blood of three cases of continued fever. Whilst this may be so, the case reported herein shows that *Bact. enteritidis* is also capable of invading the blood in children and causing continued fever of enteric type.

Summary

This paper describes a case of a child aged 5 years, an Indian evacuee from Burma, who

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PRESERVATION OF HOOKWORM OVA IN FÆCES

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ATTEMPTS have been made from time to time to find a fluid that will preserve hookworm ova in fæces sufficiently long to allow the fæces collected in the field in distant parts of the country to be forwarded to a central laboratory. In hookworm surveys, it is not always possible to examine the fæces in the field, and a field laboratory with expert microscopists entails a great deal of expenditure of money. An intelligent laboratory assistant can, however, collect fæces in the field, label them properly and forward them to a central laboratory where they can be examined in large numbers daily by centrifugalization and egg counts.

Maplestone (1929) experimented with different fluids and found that antiformin of 2 per cent strength in water was a good preservative. He says, 'This preservative does not keep all the eggs unaltered, for many showed marked degeneration especially in the specimens kept from fourteen to eighteen days, but they are easily recognized even when extensively degenerated, because counting preparations of these long-soaked stools are remarkably free from camouflage'.

In addition to the degenerating effect on the hookworm eggs, antiformin has other disadvantages. It is made from bleaching powder, the different brands of which have differing chlorine contents. Bleaching powder is very

* This work was done conjointly by the two authors, but the paper was written up by A. K. Mukerji after Dr. Maplestone left India.

(Continued from previous column)

suffered from continued fever of enteric type, in which *Bact. enteritidis* was isolated from the blood. The cultural and serological characters of the organism are described.

Acknowledgment

We have great pleasure in acknowledging our indebtedness to Major W. L. Forsyth, I.M.S. (Retired), officer-in-charge Enteric Laboratory, Kasauli, and his staff for some of the agglutination and absorption tests reported in this paper.

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unstable, so that fresh powder is required every time to prepare antiformin. Then again antiformin itself is unstable, its chlorine content diminishing gradually, so that a fresh solution has to be prepared very frequently where a large number of stools are examined over a long period of survey work.

Material and methods

Freshly passed faeces of patients with hookworm infection admitted into the Carmichael Hospital for Tropical Diseases, or of out-patients referred to this department, were received in the laboratory within 3 to 4 hours of being passed. The faeces were stirred thoroughly with a glass rod and, for the standard count, one or two 3 c.cm. samples were measured by displacement into 87 c.cm. of N/10 NaOH solution in a counting flask. Several 4 c.cm. paper containers were then filled carefully and each was dropped into a 25 c.cm. phial containing 20 c.cm. of the preservative solution under investigation after the manner described by Maplestone (*loc. cit.*). This made a 1 in 6 dilution of the faeces. The phials were corked and shaken vigorously to release the mass of the faeces from the paper container; the corks were tied to the necks of the phials with string, and the phials were kept on the laboratory shelf.

We arbitrarily fixed three weeks as the period of this experiment since we thought that this time was more than enough for the stools to reach any central laboratory from distant places where survey work was being done in this country.

After three weeks, the phials were shaken thoroughly and from each phial 6 c.cm. of the emulsion (containing 1 c.cm. of faeces) were transferred to a D.C.F. tube previously marked with a file at 6 c.cm. level. The eggs were floated in the usual manner and their condition noted.

The remaining 18 c.cm. of the emulsion in the phial (containing 3 c.cm. of stool) were poured into a counting flask and 72 c.cm. N/10 NaOH solution were added to make up the dilution to 1 in 30 for the egg count by the modified Stoll's method which has always been practised in this laboratory. From two to six counts on 0.15 c.cm. samples were done, and their average was taken and multiplied by 200 to get the number of eggs per c.cm. of the stool. For the sake of brevity the number of eggs given represents the actual number of eggs counted in 0.3 c.cm. of the emulsion; this number should be multiplied by 100 to get the number of eggs per c.cm. of the stool. When no eggs were found in 0.3 c.cm. it is indicated by zero.

When more than one phial was put up with each stool, the final count was arrived at by taking the mean egg count of the phials examined after three weeks. To get the total final count, the egg counts of the individual specimens after three weeks were added together.

In experiments with the stools kept in the preservative in a dilution of 1 in 30, 3 c.cm. of the stool were measured by displacement directly into a counting flask and the volume made up to 90 c.cm. with the preservative. The flasks were kept on the laboratory shelf throughout the period of investigation, and egg counts on 0.15 c.cm. samples were made directly from the flasks from time to time, but the initial count was always done the day after the stools were put up, to serve as a check against the standard count in NaOH solution, a flask of which with the stool was put up at the same time as the flask with preservative.

As before, two to six counts were done from each flask and their average was taken to get the number of eggs per c.cm. of the stool. The number of eggs recorded is the number of eggs actually counted in 0.3 c.cm. of the emulsion, and should be multiplied by 100 to get the number of eggs per c.cm. of the stool. As before, the egg counts of the individual stools were added together to get the total initial and final counts.

Experiments with 'Chlorion'

Searching for a better substitute for bleaching powder, we experimented with chlorion, a proprietary product made locally. This is a solution of electrolytic chlorine with an available chlorine content of 5 to 5.9 per cent, and guaranteed to keep its chlorine content over 5 per cent for three months. Antiformin was prepared from chlorion by adding 35.5 gm. of NaOH to 500 c.cm. of chlorion. A 2 per cent. solution of this antiformin in water was used for experiments. Seven different stools were put up in a dilution of 1 in 6 in phials. The initial count was 570. After three weeks the final count was 236 only. Many degenerated eggs were seen in those floated up by D.C.F. and also on the slides during the egg counts. The room temperature during these experiments ranged from 76°F. to 98°F.

It was found subsequently that chlorion already contained 10 per cent of NaOH. Thinking that the excess of NaOH added to chlorion might have an injurious effect on the eggs, we did three more experiments with chlorion diluted directly to 2 per cent with water without adding any more NaOH. The initial count was 55, and the final count was only 38. Chlorion thus showed no advantage over the ordinary bleaching powder in the form of antiformin in preserving the eggs.

Experiments with 'Perchloron'

Perchloron is a proprietary brand of bleaching powder with more available chlorine than the ordinary commercial powder. Antiformin was prepared from perchloron by adding caustic soda and anhydrous sodium bicarbonate. A 2 per cent solution of this antiformin was used as a preservative. The experiments were done during the months of June to September, when the minimum room temperature recorded was

82°F. and the maximum 98°F. Six different stools were put up in 11 phials. The initial count was 504 and the final count was 304.

In the eggs examined by D.C.F. there were many degenerated ones. 'Perchloron' therefore showed no advantage over the ordinary bleaching powder.

Experiments with Scott's 'Antiformin'

Scott (1937) recommended a special method of preparing antiformin from bleaching powder. The chlorine content in this antiformin, he says, will remain unchanged for many months in any climate, if stored in a bottle tightly corked with a slightly greased glass stopper. Antiformin was prepared exactly by the method of Scott and experiments with a 2 per cent solution were done during January to March when the laboratory temperature ranged between 70°F. and 82°F. Six experiments were done with twelve phials in dilution of 1 in 6. The initial count was 199, and after three weeks the count was 62. This result falls far short of that obtained by Scott (1937a) who found that hookworm eggs in the 2 per cent solution of antiformin prepared by him did not show any decrease up to 32 days. The temperature range in his laboratory was 18°C. to 22°C. or 64.4°F. to 71.6°F. Our experiments were conducted in a higher temperature, 70°F. to 82°F. Whether the temperature alone was responsible for the loss of eggs is not clear. We did not attempt to find out the reason of this discrepancy in results, as we were searching for a better preservative than antiformin.

Experiments with 'Paranitrophenol'

Paranitrophenol is a synthetic chemical, $C_6H_4OH(NO_2)$, with antiseptic properties. It is very sparingly soluble in water, and a saturated solution was prepared as follows:—2.5 gm. was placed in a flask with 100 c.cm. of distilled water and kept in a boiling water-bath for ten minutes with frequent shaking. After cooling and sedimentation, the supernatant fluid was filtered through filter-paper. This saturated solution was used in 5 experiments with 20 phials in dilution of 1 in 6. The initial count was 536, whereas the final count was 375, most of the eggs being degenerated. A few of the phials were examined by D.C.F. after a week of being put up, and no eggs were found. The eggs evidently were so changed in the solution that they did not float.

Experiments with Aniline Dyes

Several aniline dyes in watery solution were tested for preservation of ova. In each case faeces were put in a dilution of 1 in 6 in phials and examined after three weeks.

In 4 experiments with acriflavine 1 in 2,000 and 1 in 5,000, the count was reduced from 332 to 117 in the former and from 274 to 139 in the latter.

In methylene blue 1 in 5,000 (one experiment) the count fell from 54 to 30, and in 1 in 10,000 (3 experiments) from 111 to 68.

In 8 experiments each with brilliant green 1 in 1,000, 1 in 2,500, 1 in 5,000 and 1 in 10,000, the count fell from 725 to below 200.

In 4 experiments with mereurochrome 1 in 10,000 the count fell from 221 to 122.

Gentian violet 1 in 10,000 seemed to preserve the eggs in some experiments, but in 31 experiments the total count fell from 2,204 to 1,353.

In 9 experiments with gentian violet of the same strength but with the stool in a dilution of 1 in 30 put up in flasks, the count fell from 370 to 278.

Experiments with 'Cyllin and Dettol'

Ten experiments were done with cyllin 1 in 1,000, 1 in 2,500, 1 in 5,000 and 1 in 10,000 with stool in a dilution of 1 in 6, and 10 experiments with stool in a dilution of 1 in 30 in the same solutions. 32 to 92 per cent of the eggs were lost in three weeks.

Fifteen experiments with dettol 1 in 1,000, 1 in 2,500 and 1 in 5,000 with stools in dilutions of 1 in 6 and 1 in 30 gave the same result; the eggs were not preserved.

Experiments with 'Thymol'

One gramme of powdered thymol was mixed with one litre of hot distilled water and shaken frequently. Complete solution was effected by the next day. This stock solution was further diluted by distilled water to make the weaker solutions. Ten experiments were done with 1 in 1,000, 1 in 2,000, 1 in 3,000, 1 in 4,000 and 1 in 5,000 with stools in dilutions of 1 in 6 and 1 in 30. More than half the eggs were lost in three weeks.

Experiments with 'Formalin'

Formalin containing 40 per cent formaldehyde was diluted with water to 0.5, 1 and 2 per cent, and stools were diluted 1 in 6 and 1 in 30. The count fell and the eggs degenerated.

Experiments with 'Formalin-saline'

The next set of experiments was made with 1, 2, 3 and 4 per cent formalin in 1 per cent solution of sodium chloride in dilutions of 1 in 6 and 1 in 30. The count fell but not markedly. In these experiments it was noticed that the eggs kept very well in the control phials of 1 per cent NaCl solution and that the eggs floated up by D.C.F. looked quite fresh. So the next experiments were done with 1 per cent NaCl only.

Experiments with 1 per cent NaCl solution

Ten grammes of common salt were dissolved in 1 litre of tap water. A few trials made with the solution in distilled water did not show any improvement in results.

In the first series of 10 experiments conducted between July and October, 10 different stools were put up in phials in a dilution of 1 in

6, and 8 of these stools were also put up in flasks in a dilution of 1 in 30.

The total initial count was 1,109. After three weeks the total final count was 1,001 indicating a loss of only 9.7 per cent.

In the flasks, the initial count was 1,036, and the final count 1,106; evidently there was no loss. The better result was probably due to prolonged soaking of the faeces in the flasks in plenty of salt solution and to less handling of the specimens as the counts were made directly from the flasks in which the stools were originally put up.

The experiments were discontinued in the winter months as we had already found by experience that hookworm eggs kept well in low temperatures. This has also been noticed by Scott (1937a) who found that the hookworm eggs did not show any great decrease up to 32 days even in distilled water in a temperature of 18°C. to 22°C., i.e., 64.4°F. to 71.6°F. We resumed our experiments in March when the minimum temperature of our laboratory rose up to 76°F.

In the second series, 23 experiments were done between March and November. Twenty-three different stools were all put up in phials only in a dilution of 1 in 6. Loss of eggs in individual experiments began to be noticed in the early part of the series. In 2 experiments the count fell from 50 and 51 to 38 and 36, and in one experiment from 34 to 2. This last stool had also been put up in a flask in a dilution of 1 in 30, when the count fell only from 34 to 32. In one experiment in which the stool was very fatty, the count fell from 30 to 1.

We had noticed previously that fermentation of the stools in the phials caused bubbles of gas to force up the stools near the corks, where a part remained out of the salt solution. Thinking that the eggs in this part of the stool might be lost, we did 4 comparative experiments with stools in a dilution of 1 in 6 in 40 c.cm. phials and in 25 c.cm. phials, the quantity of the stool and the preservative being the same in each, i.e., 4 c.cm. and 20 c.cm. The results were no better. The count fell from 438 to below 300.

It is well known that fermentative changes going on in the stools after they have been passed, increase the acidity of the stools. To find out whether the reaction of the stools changes after three weeks, we did the following experiments in 7 samples of different stools. The phials were filled with faeces and freshly prepared salt solution in distilled water, and immediately afterwards one phial was thoroughly shaken and 10 c.cm. was centrifuged. The supernatant fluid was tested for pH by Hellige's colorimeter. Seven different stools tested in this way showed reactions as follows:—6.9, 6.8, 7.0, 6.0, 6.5, 6.0, 6.0, i.e., all were more or less acid except one. This is what we had expected, as the patients from whom the stools were collected were all Indian in-patients, who were on a mixed diet with excess of starch and fats. Moreover,

all these patients had moderately heavy hookworm infection, which causes a catarrhal condition of the upper bowel; this factor also gives rise to acid stools. It is also known that hookworm infection causes imperfect digestion of carbohydrates. Intestinal fermentation associated with imperfect digestion of carbohydrates and formation of lower fatty acids e.g., acetic, lactic and butyric, causes the stools to become acid. An excess of fats in the faeces also gives rise to an acid reaction (Cambridge, 1914).

Those seven phials were tested again for pH and for eggs after three weeks. The results shown below are interesting:—

TABLE I

Number	Initial pH	Final pH	Reduction in pH	Initial count	Final count
27	6.9	5.2	1.7	185	39
28	6.8	6.0	0.8	109	15
29	7.0	5.8	1.2	127	82
30	6.0	5.1	0.9	477	181
31	6.5	6.2	0.3	93	107
32	6.0	5.8	0.2	174	182
33	6.0	5.8	0.2	83	91

It will be seen that the less the change in reaction, the better is the preservation. Reduction of pH over 0.3 resulted in loss of eggs.

To find out whether the addition of sodium chloride had any effect on the pH, the same seven stools were put up at the same time in phials of distilled water also as control. The result is shown below. The number of eggs recovered is also given to show that the eggs are not preserved in distilled water at a temperature of over 80°F., in which these experiments were done.

TABLE II

Experiment number	Initial pH	Final pH	Initial count	Final count
27	6.8	5.2	185	4
28	6.8	6.0	109	0
29	7.0	6.0	127	37
30	6.0	5.2	477	64
31	6.5	6.2	93	42
32	6.2	5.8	174	106
33	6.0	5.4	83	59

This shows that sodium chloride *per se* had no effect on the increasing acidity of the stools.

Experiments with buffered salt solutions

In the last 2 experiments (32 and 33) in this series, a buffer solution was added to the stools to see if it would stop the increasing acidity. The buffer solution was prepared by mixing 50 parts of M/15 Na₂HPO₄ and 33 parts of M/15 KH₂PO₄. The pH of this mixture was found to be 7.0. One gramme of sodium chloride was added to 100 c.cm. of the buffer solution

and two stools were put up in phials in the buffered salt solution, in a dilution of 1 in 6. In both experiments the pH was reduced from 6.2 to 5.6 in three weeks, without loss of eggs. Reduction of pH to 0.6 did not thus result in loss of eggs. The buffered salt solution had, however, no effect in maintaining the pH. Since however the eggs were preserved, 4 more experiments were done with the same solution with the following results:—

TABLE III

Experiment number	Initial count	FINAL COUNTS	
		1 per cent salt solution	1 per cent buffered salt solution
34	69	0	22
35	208	223	216
36	46	1	12
37	20	22	13

The eggs were all lost in 1 per cent salt solution in experiments 34 and 36. These 2 stools were full of fat which probably explains the loss, as an excess of fats in the faeces gives rise to acid reaction. Buffered salt solution had, then, no effect on preservation of eggs in fatty stools. We did not try the effect of pure buffer solution (without NaCl) on preservation, as we were attempting to find a simple method of preservation not involving much chemistry.

The next step was to find out if sodium bicarbonate would neutralize the acidity and preserve the eggs. Twenty-two experiments were done with 1 per cent salt solution and with 1 per cent sodium bicarbonate solution in a dilution of 1 in 6. The initial count was 2,646, and it fell to 1,743 in salt solution and to 1,829 in sodium bicarbonate.

Eighteen experiments were done with a solution containing 1 per cent salt and 1 per cent sodium bicarbonate. The count fell from 2,303 to 1,497 in salt and to 1,601 in bicarbonate.

The final result of 55 experiments with 1 per cent salt solution only with stool in a dilution of 1 in 6 showed that from a total initial count of 5,994, the fall was to 4,012.

For the sake of comparison, the results of the three different solutions are given together as follows:—

TABLE IV

Solution	Number of experiments	Initial count	Final count
1 per cent salt ..	55	5,994	4,012
1 " " soda ..	22	2,646	1,829
1 " " salt-soda ..	18	2,303	1,601

It was evident that the eggs were not preserved in any of the above solutions with the stools in a dilution of 1 in 6.

Seventeen experiments were done with 2 per cent salt solution in phials and 4 experiments

in flasks. Counts fell markedly. Four experiments with 3 per cent salt solution showed even worse results.

Experiments with 1 per cent salt solution with stool in a dilution of 1 in 30

In the first series of 10 experiments, 8 stools were put up in a dilution of 1 in 30, and counts fell from 1,109 to 1,106. Eggs were well preserved (*vide ante*). In the second series of 23 experiments we tried a 1 in 6 dilution, but we found that this dilution did not work. Therefore in later experiments we reverted to a dilution of 1 in 30. In these experiments the final count was slightly higher than the initial count. Adding together the results of 23 experiments, we found that the initial counts totalled 2,702 and the final counts 2,820.

Fifteen stools were put up in the same dilution in 1 per cent sodium bicarbonate solution and also in 1 per cent salt-soda solution. The fall in egg counts in both these solutions was slight, but the eggs were not quite so well preserved as in salt solution.

The individual counts of the 23 experiments of 1 per cent salt solution in 1 in 30 dilution are given below.

TABLE V

Serial number	Experiment number	Initial count	Final count
1	2	158	195
2	4	8	12
3	5	57	63
4	6	16	14
5	7	236	204
6	8	76	77
7	9	332	327
8	10	153	124
9	41	125	152
10	42	183	196
11	43	212	203
12	44	204	185
13	45	22	24
14	46	319	337
15	47	58	67
16	48	15	16
17	49	12	12
18	50	103	106
19	51	72	73
20	52	246	263
21	53	29	22
22	54	49	39
23	55	17	19

It appears therefore that sodium chloride in 1 per cent strength has a powerful effect in preserving hookworm ova if the stools are put up in a dilution of 1 in 30.

A noticeable feature of the preservation in the salt solution is that the eggs look quite fresh even after three weeks and only occasionally one or two degenerated eggs are seen. Out of 2,820 eggs recovered after three weeks, only 34 eggs looked degenerated, but even then these eggs were quite distinguishable.

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THE EFFECT OF INDIAN-MADE MEPACRINE HYDROCHLORIDE* ON *PLASMODIUM KNOWLESI*

By B. M. DAS GUPTA

and

L. B. SIDDONS

Department of Protozoology, School of Tropical Medicine, Calcutta

THE satisfactory results obtained in the treatment of bird malaria (*P. relictum*) with mepacrine hydrochloride (Das Gupta and Siddons, 1943) encouraged us to try it in *P. knowlesi* infection in the monkey, *Silenus rhesus*. It is well known that, in this monkey, this parasite produces the most intense infection which, if unchecked, usually terminates fatally. Therefore, infected monkeys are very suitable for testing the anti-malarial properties of a drug. Mepacrine is the British Pharmacopoeial name for atebirin which has been shown to be effective against *P. knowlesi*.

* Prepared by Bengal Chemical and Pharmaceutical Works Ltd., Calcutta.

(Continued from previous page)

Some of the flasks were examined at intervals from the fourth week onwards, and it was found that the eggs begin to degenerate from after 28 days and gradually diminish in number.

All these 23 experiments were done during the period of March to November, the laboratory room temperature varying between 76°F. and 97°F. or 24.4°C. to 36.1°C.

Summary

A solution of common salt in 1 per cent strength preserves the hookworm ova, when the stool is diluted 1 in 30 with the solution. The eggs are well preserved up to three weeks and then begin to degenerate. In this solution the eggs look quite fresh. Stools collected in the field can be measured into 3 c.cm. paper containers and dropped into suitable bottles containing 87 c.cm. of 1 per cent solution of common salt in water, or the stools may be measured by displacement into the bottles. If the bottles are well corked, they should reach the central laboratory in good condition. In the laboratory, egg counts can be made directly from the flasks and if no eggs are found, 30 c.cm. can be centrifuged and the eggs, if any, floated up by D.C.F. For safety the corks should be tied to the necks of the bottles before they leave the field.

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Methods

Five monkeys (*S. rhesus*) were used in these tests: two (nos. 1 and 2), infected with a strain of *P. knowlesi*, were received through the courtesy of the Malaria Institute, New Delhi, and three (nos. 3, 4 and 5) were inoculated in our laboratory by the intra-peritoneal route with parasitized blood from no. 2. All the animals showed typical infection when treatment was begun. The weights of the monkeys varied between 2 and 6 kilogrammes.

The drug was administered by intramuscular injection. Doses, given once daily, contained 0.025 gm. dissolved in half a cubic centimetre of distilled water. This was the dosage of atebirin which Chopra and Das Gupta (1933) found to be both effective and well tolerated by the monkeys of average weight.

Blood smears were examined daily during the patent period, and the infection-rate of the red blood cells was determined by counting 500 or 1,000 cells, the numbers depending on the intensity of the infection. After the first negative smear, the smears were taken at intervals of not more than five days.

Results

Experiment no. 1.—Monkey 1, which came from Delhi, first showed parasites four days after its arrival in our laboratory. It was treated on the third day of the patent period when the infection-rate of the red blood cells was less than 0.1 per cent. On the fourth day it received a second dose, the infection-rate being still less than 0.1 per cent. The following day only extremely scanty degenerating parasites were observed, whereupon treatment was suspended. The blood became negative on the sixth day after the first appearance of parasites. Parasites were again found after a latent period of between ten and fourteen days.

Experiment no. 2.—Monkey 2, also from Delhi, showed parasites on arrival in the laboratory. It was not treated till a very advanced stage of the infection had been reached, as other animals were not available for sub-inoculation, and no. 1 was still negative. The infection rate of the red blood cells at the time treatment was commenced was 41 per cent. A dose of 0.025 gm. of the drug failed to save the animal, which was found dead the next morning.

Experiment no. 3.—Monkey 3 was treated from the third day of the patent period, when the infection-rate of the red cells was 1.6 per cent. It received three doses given on consecutive days. After the first dose, the infection-rate was much the same, 1.3 per cent, but at least 50 per cent of the parasites were abnormal in morphology. These appeared to be disintegrating and were badly stained, and some being devoid of pigment. Abnormal clumping of the pigment was observed in forms other than mature schizonts, including gametocytes. After the second dose, the parasites decreased in number and the blood became negative after the third

dose. Parasites reappeared after a latent period of eleven days.

Experiment no. 4.—Two monkeys, 4 and 5, of approximately the same weight, were inoculated with the same quantity of parasitized blood taken on the same occasion from monkey 2. Monkey 5 showed parasites a day earlier than monkey 4. It was treated when monkey 4, which was kept as a control, was also found positive. The course of the infections in the two animals from the date of treatment is shown in the following tabular summary:—

Date	MONKEY 4 (UNTREATED CONTROL)	MONKEY 5, TREATED	Treatment
	Infection rate of r.b.c.	Infection rate of r.b.c.	
12-12-42	0.5 per cent	4.6 per cent	0.025 gm. of drug.
13-12-42	5.4 per cent	1.4 per cent (Mostly de- generating parasites.)	0.025 gm. of drug.
14-12-42	11.0 per cent	Less than 1 per cent. (Degen- erating forms only.)	
15-12-42	45.0 per cent (Animal died.)	Nil	
16-12-42	..	Nil	
17-12-42	..	Nil	
21-12-42	..	Less than 0.1 per cent.	

The infection took a normal course in monkey 4, terminating fatally, while in monkey 5 it was controlled by the timely administration of mepacrine hydrochloride. Parasites in small numbers reappeared in the blood after a latent period of only six days.

Summary of results

Of four monkeys (*S. rhesus*) infected with *P. knowlesi* and treated with mepacrine hydrochloride during the patent period, three have survived. In the case of the failure, treatment could hardly be expected to save the animal when the red cells had already been parasitized to the enormous extent of 41 per cent. In the surviving monkeys the drug controlled the infection and was observed to have a destructive action on the parasites. Both schizogony and gametogony were affected, and the peripheral blood was rapidly cleared of all forms of the parasite; the dosage employed (0.025 gm. daily for two or three days) failed however to prevent relapses, and the monkeys all showed parasites after latent periods varying from six to fourteen days.

Comments

This mepacrine hydrochloride made in India is evidently quite similar to atebirin in its effect on *P. Knowlesi*. Chopra and Das Gupta (*loc. cit.*)

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LIVER FUNCTION AND BLOOD VITAMIN C IN SECONDARY SYPHILIS

By K. D. LAHIRI, M.B., B.S.

From the Skin and Venereal Department, Patna Medical College Hospital

THE spread in the body of the infection of syphilis is very rapid; so much so that Lees (1937) has observed that by the time the primary lesion has developed, the disease is practically always generalized. The spread of the *Treponema pallida* is by various routes such as lymph vessels, perivascular lymphatics and the blood stream. The dissemination takes place after a certain period to all parts of the body, and no tissue is immune from its attack. The skin surface shows the evidence of generalization of the attack in six to ten weeks' time. The early skin eruptions of syphilis are symmetrically distributed and are generalized, but when the skin lesions appear late they are localized. Different patients show differences in the type of the skin eruption which may depend on variations in the virulence of the spirochæte, and in the resistance of the tissues of the host as shown by the reaction of skin to the infection.

Curiously enough, I found, in in-patients in the Patna Medical College Hospital, that over 50 per cent of syphilitic patients developing symptoms of arsenical intolerance were suffering from secondary syphilis. Irgang (1937) emphasizes that the tests for the hepatic function should be performed whenever a patient reacts abnormally to the arsphenamines. Lahiri (1942) has found that the blood vitamin C content is reduced in syphilis.

Observation

The present work was undertaken to find out whether the detoxicating mechanisms of the body are seriously and equally affected. The

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showed that atebirin has a powerful destructive action on this parasite, inhibiting the multiplication of all forms in the peripheral blood, which is soon freed of its infection. However, as with mepacrine hydrochloride, relapses invariably occurred in cases treated for two to four days. In their tests Chopra and Das Gupta observed that the parasites temporarily disappeared for periods varying from two to fifteen days. If the number of tests, number of doses, density of parasites before treatment, and intervals between successive examinations in the work of Chopra and Das Gupta and in the present work are taken into consideration, it does not appear that the periods of latency following treatment with atebirin and with mepacrine hydrochloride differ significantly.

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liver function and the blood vitamin C content in 42 cases of secondary syphilis were investigated.

TABLE I

Liver function and blood vitamin C content of secondary syphilitics. No reaction observed with arsenic therapy

Case number	Age	Diet	Hippuric acid in gm. excreted in urine	Vitamin C in mg. per 100 c.cm. blood	Duration of treatment before disappearance of rash
1	18	Vegetable	3.42	0.50	4½ weeks
2	34	Mixed	2.96	0.41	6 "
3	44	Do.	2.87	0.37	6 "
4	37	Do.	3.21	0.40	5 "
5	38	Do.	3.20	0.41	5½ "
6	17	Vegetable	2.84	0.39	6½ "
7	27	Do.	2.42	0.51	7 "
8	32	Mixed	2.31	0.42	6½ "
9	28	Do.	2.01	0.43	6 "
10	38	Do.	2.89	0.41	5 "
11	45	Do.	2.34	0.56	7 "
12	42	Do.	2.09	0.52	6½ "
13	15	Vegetable	3.14	0.58	5½ "
14	30	Do.	2.64	0.52	5 "
15	22	Mixed	2.84	0.37	6½ "
16	27	Do.	3.04	0.42	6 "
17	19	Do.	2.75	0.27	7 "
18	38	Do.	3.44	0.30	7 "
19	22	Do.	3.45	0.22	7 "
20	36	Do.	3.21	0.44	6 "

It has long been recognized from experiments on animals that when the liver is damaged its detoxicating function is reduced. One of the methods employed in measuring the detoxicating function of the liver is the determination of the amount of hippuric acid synthesized by the liver and excreted in the urine after a test dose of sodium benzoate. Quick (1931) was the first to make use of this test in studying the detoxifying function of the liver in man. In normal individuals in other countries the test has been used by Snell and Plunkett (1936), Boyce (1939), Bartels (1938), Schmidt *et al.* (1941), Ziffren *et al.* (1942) and in Indians by Lahiri (1942).

The method employed for the estimation of blood vitamin C was that of Tillmans *et al.* (1932) and Farmer, Abt and Aron (1940). The method was slightly modified by Lahiri and Rudra (1942).

The liver function was tested by the method of Lahiri (1942) and the blood vitamin C content by the method of Lahiri and Rudra (*loc. cit.*): (a) in 20 cases of secondary syphilis without arsenical reaction (table I), (b) 24 cases of secondary syphilis developing reactions, in which arsenic injections were continued but preceded by the injection intravenously of 300 mg. of vitamin C (table II), (c) in 8 cases of secondary syphilis all developing symptoms of grave arsenical intolerance (table III), observations being made on the results of resuming anti-syphilitic treatment with arsenic

TABLE II

Liver function and blood vitamin C content of secondary syphilitics showing mild intolerance with anti-syphilitic therapy. Arsenic injections continued with 300 mg. of vitamin C

Case number	Age	Diet	Hippuric acid in gm. excreted in urine	Vitamin C in mg. per 100 c.cm. blood	RESULT OF ARSENIC THERAPY		Duration of treatment before disappearance of rash
					Alone	With vitamin C	
1	17	Vegetable	3.88	0.42	Reaction	No reaction	3½ weeks
2	31	Do.	3.84	0.47	Do.	Do.	4 "
3	22	Mixed	2.08	0.31	Do.	Do.	4 "
4	62	Do.	2.14	0.31	Do.	Do.	3½ "
5	44	Do.	2.00	0.40	Do.	Do.	3 "
6	21	Do.	2.11	0.32	Do.	Do.	4½ "
7	54	Do.	2.00	0.40	Do.	Do.	3½ "
8	31	Vegetable	2.47	0.31	Do.	Do.	3 "
9	28	Mixed	3.14	0.21	Do.	Do.	3 "
10	44	Do.	2.78	0.25	Do.	Do.	3 "
11	32	Do.	2.90	0.33	Do.	Do.	3 "
12	34	Do.	2.43	0.31	Do.	Do.	4½ "
13	40	Do.	3.40	0.24	Do.	Do.	3½ "
14	34	Do.	2.76	0.22	Do.	Do.	3 "
15	35	Do.	3.75	0.20	Do.	Do.	3 "
16	47	Do.	3.21	0.28	Do.	Do.	3 "
17	52	Vegetable	3.02	0.32	Do.	Do.	3 "
18	31	Do.	2.76	0.40	Do.	Do.	2½ "
19	46	Mixed	2.04	0.26	Do.	Do.	4½ "
20	50	Do.	2.08	0.21	Do.	Do.	4 "
21	39	Do.	2.43	0.27	Do.	Do.	3 "
22	61	Do.	3.00	0.24	Do.	Do.	2½ "
23	43	Do.	2.09	0.29	Do.	Do.	3 "
24	24	Vegetable	3.40	0.34	Do.	Do.	3½ "

TABLE III

Liver function and blood vitamin C in secondary syphilitics. All developed grave symptoms of arsenical intolerance

Case number	Age	Diet	Hippuric acid in gm. excreted in urine	Vitamin C in mg. per 100 c.cm. blood	Symptoms
1	42	Vegetable	3.07	0.24	Dermatitis.
2	50	Mixed	3.12	0.30	Do.
3	27	Do.	2.84	0.17	Jaundice.
4	33	Do.	2.02	0.20	Dermatitis.
5	37	Do.	2.14	0.14	Do.
6	32	Do.	2.04	0.18	Jaundice.
7	52	Do.	2.12	0.13	Do.
8	54	Do.	2.03	0.22	Dermatitis.

TABLE IV

Liver function and blood vitamin C in secondary syphilitics 3 months after treatment with liver extract (3,000 gm. I.M.) daily and vitamin C (300 mg. I.V.) daily for 12 days

Case number	HIPPURIC ACID IN GM.		VITAMIN C IN MG. PER 100 C.C.M. OF BLOOD		Result with anti-syphilitic therapy
	Before treatment	After treatment	Before treatment	After treatment	
1	3.07	3.47	0.24	0.54	No relapse.
2	3.12	3.64	0.30	0.46	Do.
3	2.84	3.20	0.17	0.34	Do.
4	2.02	3.00	0.20	0.46	Do.
5	2.14	2.64	0.14	0.32	Do.
6	2.04	2.42	0.18	0.37	Do.
7	2.12	2.65	0.13	0.27	Jaundice.
8	2.03	2.44	0.22	0.40	No relapse.

in all the 8 cases of grave arsenical intolerance after treating them with liver extract (3,000 gm. intramuscularly) and vitamin C (300 mg. intravenously) for 12 days (table IV).

The times of the disappearance of the skin eruptions in patients undergoing anti-syphilitic therapy with and without vitamin C have been observed and compared (tables I and II).

Conclusion

In syphilitic infection the liver function is impaired and also the vitamin C level of blood is lowered. Bundesen *et al.* (1941) found that among the various substances acting as detoxifying agents, vitamin C stands in a unique position. While most other substances are products foreign to the body, ascorbic acid is one of the most powerful physiological reducing agents. Since the physiological reducing power of patients with secondary syphilis is damaged by the abnormal lowering of the level of the blood vitamin C, there frequently occurs mild intolerance to arsenic, and not uncommonly grave symptoms occur.

The hippuric acid excretion in normal Indians has been found by Lahiri (1942) to be 5.0 gm. By various authors in different diseases the hippuric acid excretion has been found to be much lowered, and Lahiri (1942) has found it to be lowered in both acquired and congenital syphilis. From the present investigation it appears that the liver function in cases of secondary syphilis, although impaired, is less affected than in unselected cases of syphilis. Lahiri (1942) has found the blood vitamin C content in normal Indians varying from 0.6 mg. to 2.2 mg. per 100 c.cm. of blood. Lahiri (1942) has found the vitamin C content of blood much diminished in both acquired and congenital syphilis. The present investigation shows that the average blood vitamin C content in secondary syphilis is at a lower level than in unselected cases of syphilis. The injection of arsphenamines further lowers the blood vitamin C level; thus the physiological detoxicating power of the blood exerted by its vitamin C content is so much reduced in cases of secondary syphilis that arsenical intolerance commonly occurs in these cases. Many workers have found by laboratory research and also by actual clinical studies that the toxicity of 'chemotherapeutic drugs may be reduced by simultaneously giving with them certain other substances which exert a detoxicating action, and even in 1909 Ehrlich pointed out that 'reduction' is the most important chemical reaction in the detoxifying process of chemotherapeutic agents, especially the arsphenamines. Lahiri (1941) observed the beneficial action in arsenical dermatitis of injections of liver extract and vitamin C. Sulzberger and Oser (1935) while working with guinea-pigs first observed the influence of the vitamin C of the diet on sensitization to arsphenamines. Dainow (1937) recommended vitamin C for the detoxification of arsphenamine in human therapy, and has been supported by a host of workers such as Landfish (1937), Lahiri (1941; 1942) and Bundesen *et al.* (*loc. cit.*).

Summary

In secondary syphilis the administration of vitamin C together with the routine treatment with arsenic and bismuth is very helpful as a safeguard against the development of arsenical intolerance, and helps the early cure of skin rashes.

Acknowledgments

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ZINC IONIZATION IN ECZEMA AND SUPERFICIAL DERMATOSES

By M. P. MATHUR, M.B., B.S., D.M.R.E.

Kotah

ZINC is extensively used in medicine for treating skin diseases. It is commonly employed in the form of ointments, lotions and dusting powders. In all these forms of treatment, absorption and penetration are little so that the results are achieved only slowly. By zinc ionization these ions are made to migrate deeper into the tissues in a nascent state. The therapeutic effects, therefore, are carried deeper into the tissues and the ionic state makes them much more effective. Ionization should therefore be more effective than any other method in vogue.

Cases treated by zinc ionization were mostly chronic and resistant to other forms of treatment. One case in particular was of 14 years' duration. In all these cases two factors were common: the cause of the condition was not apparent, and itching was a prominent feature. It was for the latter that the patients presented themselves for treatment. Very often this

itching would lead to ulcer formation or to weeping. Broadly speaking, therefore, the patients presented themselves in one of the three stages :—

(1) Simple patches with marked pigmentation, cutaneous hypertrophy and marks of scratching.

(2) Weeping stage with or without 'crust' formation.

(3) Ulcerative stage with or without sepsis. Zinc ionization was tried in all these types.

Method of application

Ionization current is conveniently derived from a Schall's pantostat or any other convenient source. Thin plates of zinc are used because zinc is a brittle metal and if thick cannot be moulded to the patch. The method of application of the positive plate differed slightly in the three types.

Where the skin is intact the plate is applied directly. In the crusted type, oily preparations are applied for a few days to remove the crust. In ulcerative forms, a thin padding of absorbent cotton soaked in 2 per cent zinc sulphate solution is applied to the surface to cover the irregularities of surface. A zinc plate is applied over it and the whole is dipped in 2 per cent zinc sulphate solution or the solution is continuously irrigated over it to keep the padding moist. Since most of the lesions were in the hands, legs and feet, this could be easily done. But for places like the groin, where this method is troublesome, the plate can be directly put over the patch irrespective of ulceration, etc. The wet method is the method of choice wherever it is possible, for it gives better conduction and so better results.

The positive plate is a thin zinc one and is easily available in the market. Thinness of the plate allows good moulding.

The negative plate is a lead plate as is used in diathermy work. This plate requires careful adjustment, or the limb will be thrown into spasmodic twitches. Hydroxyl ions, too, are liable to produce their caustic action if sufficient care is not taken. I use as a negative plate a flat wooden board, 1 foot by 6 inches, to which a lead sheet is fixed. A butterfly screw is fixed at one end to secure the lead from the pantostat. A moist piece of flannel or lint is evenly spread over the plate, and one foot is firmly placed over it. The butterfly screw should not directly come in contact with the foot. If twitchings occur, the flannel should be smoothed or only the heel should be kept in contact with the flannel.

The following is a description of the actual procedure on a case with a patch on his right shin :—

The patient is seated on a bench and his right foot is placed in an enamelled basin placed on the same bench. His left foot is placed on the negative plate placed on the floor. The commercial packings of absorbent cotton are in the form of the compressed laminæ and one or two

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laminæ can be taken from a roll, cut to size and applied to the patch. Zinc sulphate solution is poured over the patch so that the cotton is soaked and the superfluous fluid collects in the basin. A zinc plate of the size of the patch is placed over the cotton, and the lead from the terminal of the pantostat is secured to the lower margin of the plate by means of a diathermy clip. It is an advantage to put a small rubber sheet between the clip and the skin. The clip is secured to the lower margin so that the current must pass through the patch. Oiled silk, as available in any operation room, or rubber sheet is placed over the zinc plate and the whole is firmly but gently pressed against the patch by the patient's left hand. The oiled silk or rubber prevents the hand from coming in conducting communication with the plate. In his right hand, the patient takes a big swab of absorbent cotton, dips it in the basin and squeezes it over the upper margin of the patch. The cotton padding is thus continuously soaked without any inconvenience of splashing. The current is very slowly increased till the patient's limits of tolerance are reached. This is usually attained between 10 to 20 milliamperes. This current is passed for 15 to 20 minutes. During the passage of the current, the patient feels as if 'ants are biting' and this sensation usually persists for $\frac{1}{2}$ to 2 hours. This sensation does not make him uncomfortable. A successful ionization is judged by a faint whiteness over the patch—'ionization whiteness'. The negative plate is moistened once or twice with tap water. This plate can also be applied to the back instead of the foot.

In mild cases, twice a week is sufficient; in severe cases, three times a week or more if necessary.

Relief in symptoms is marked. The itch is definitely less after the very first sitting and after three or more sittings it is no longer felt. It is better, however, to give a few more sittings even after complete relief. A severe lesion may at first pass into the weeping stage. In such cases, the frequency of ionization should be increased and the exudate will be reduced. Ulcers require no dressings because ionization dries up the ulcer and gives it a protective covering of ionization whiteness. Sepsis is also overcome by ionization alone. If necessary, however, suitable dressings can be applied after ionization.

Case 1.—H. M., 60 years, had a patch on his right shin, 5 inches by 3 inches. Duration 14 years. When first seen, the patch was full of septic scratches. After the first sitting, itching was definitely less. After three sittings, the patch passed into weeping stage. The condition cleared up after ten or twelve sittings. There has been no recrudescence in the last eight months.

Case 2.—H. M., 20 years. Patch on his right shin in the form of a cuff in the lower one-third. The patch was covered with thick crusts and was septic at places. A preliminary treatment with ultra-violet rays and zinc ointment was given for a week. After this, zinc ionization was given. After the fourth sitting, there was no pain or itch and the patch had cleared up.

(Concluded at foot of next column).

SEASONAL PERIODICITY OF PLASMODIA OF MALARIA AT GIRIULLA, CEYLON

By V. SIVALINGAM, M.R.C.P., D.T.M. & H.

Parasitologist, Department of Medical and Sanitary Services, Ceylon

OBSERVATIONS over an adequate period to determine the behaviour of malaria parasites during the different seasons of the year had not previously been made in Ceylon. This report is based on the findings of observations made regularly from 3rd October, 1938 to 29th November, 1941, at village Giriulla, Ceylon.

The method was to make weekly visits to the out-patients' department at Giriulla Government Hospital and secure 'thin' and 'thick' smears from patients who were taking treatment for malaria. The films were examined at the central laboratory in Colombo. The number of films examined was 3,889, of which 1,926 showed parasites.

The attached graph shows the results. The relative species prevalence is shown monthly; the graph also shows the weekly malaria attendance at the out-patients' dispensary. In mixed infections, each of the species present was counted.

The following points are noticeable:—

(1) There is a marked fluctuation of the three parasites found in Ceylon. The benign tertian and sub-tertian increase or decrease together, while the quartan behaves in the opposite way.

(2) Quartan was high in October, November and December 1938 varying between 60 to 80 per cent; sub-tertian was lowest with 15 per cent and tertian was intermediate with 40 per cent. The morbidity curve shows low malaria incidence during these months.

(3) The rise in malaria incidence between January and February 1939 is to be noted. The quartan drops to 30 per cent and sub-tertian rises to 45 per cent.

(4) When the morbidity rose steeply in April 1939, i.e., the onset of the 1939 malaria

(Continued from previous column)

Conclusions

Zinc ionization has a definite advantage over other treatments in that it is simple to apply, gives quick relief and rids the patient of the greasy dressings and lotions which are a source of trouble to the patient. The curative value of the ionization has yet to be assessed because of the shortness of the period of observation. In only a few cases was there recurrence, but this was of a mild type and yielded very soon. Even the ulcerative types do not require dressing after one or two sittings. Ionization and a dusting powder consisting of zinc, boric and starch suffice in most of the cases.

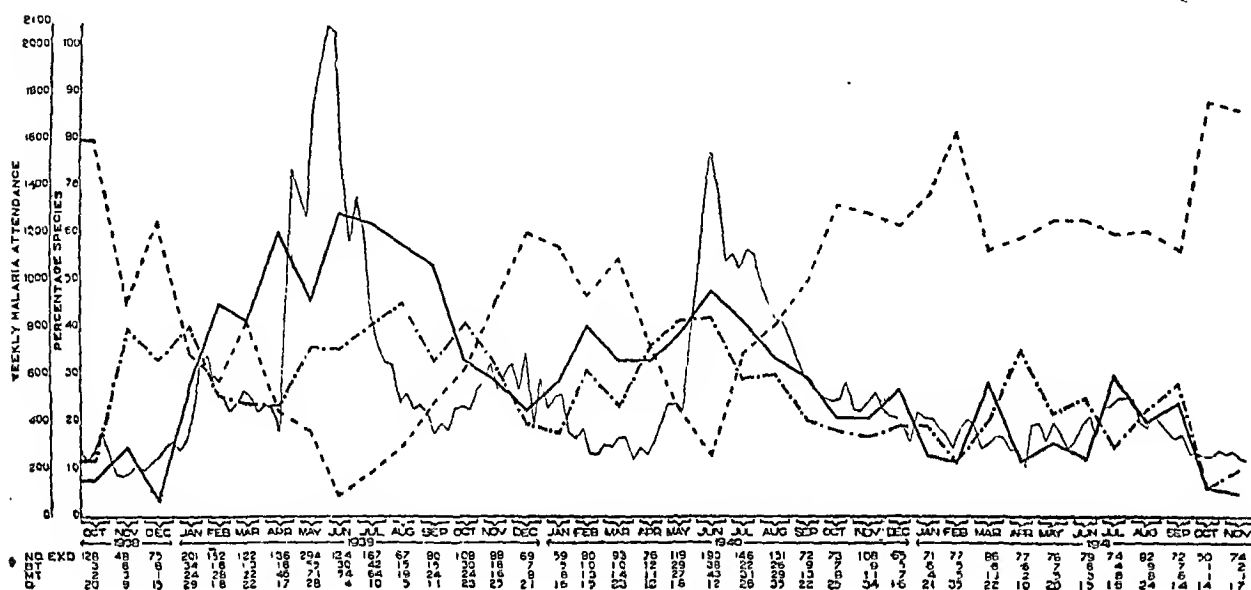
epidemic, and reached its peak in June, the quartan prevalence was lowest with 5 per cent and sub-tertian was highest with 65 per cent.

(5) When the epidemic was declining in July, quartan began to increase, and reached 60 per cent in December 1939. Then it maintained its high position until the end of March 1940. Malaria morbidity was low during the whole of this period.

were taken from a population of about 162 on 10th February and 4th March, 1941. The results were B.T. 4 (26 per cent), M.T. 2 (13 per cent), and Q. 9 (60 per cent). These findings showing the dominant position of quartan and the low place of malignant tertian are in accord with the results obtained from observations made on the sick at the dispensary. Therefore it is inferred that the findings for the

RELATIVE PERCENTAGE SPECIES PREVALENCE-GIRIULLA

BENIGN TERTIAN
MALIGNANT TERTIAN
QUARTAN
WEEKLY MALARIA ATTENDANCE



(6) From April 1940 quartan decreased until it reached its lowest in June. The great increase in malaria morbidity during this period is to be noted.

(7) Quartan rose again and in December 1940 it was 62 per cent. The malaria morbidity was again low.

(8) Throughout the year 1941, quartan was the predominant species ranging between 87 per cent and 56 per cent, while sub-tertian did not exceed 30 per cent during the period.

(9) The malaria morbidity curve shows two outbreaks of malaria during the period of the observations. During each peak, the quartan occupied a characteristic bottom position; the greater the rise in malaria morbidity, the lower the quartan. From the curves it is evident that benign tertian and sub-tertian are together responsible for malaria outbreaks in this locality.

In order to decide that these findings were not fortuitous but reflected the true relative incidence of malaria parasites in Giriulla area, house to house visits were made in a locality two miles from Giriulla Hospital. Blood smears were made from the inmates, irrespective of whether they were healthy or sick. Eighty-five samples

out-patients truly reflected the position in the villages themselves in the area.

Conclusions

1. There is a marked seasonal species incidence of malaria parasites.
2. The parasites responsible for epidemic outbreaks are B.T. and M.T., the latter particularly playing a dominant rôle.
3. The quartan parasite dominates over the other two at periods of the year when malaria is low and static.
4. Sub-tertian and quartan behave inversely in their relative prevalence throughout the year.
5. B.T. accompanies the M.T. parasite in its ups and downs throughout the year.
6. The low relative prevalence of the quartan parasite on one hand, and a high sub-tertian parasite incidence on the other, appear to be an indication of an approaching malaria outbreak—seasonal rise and epidemic. The presence of quartan at 50 per cent or more would seem to be an indication of a healthy season, while the increase of M.T. to 50 per cent or over appears to serve as a warning of an oncoming outbreak of malaria.

BREEDING OF *CHRYSOMYIA MEGACEPHALA* IN CLOSED SEPTIC TANKS

By M. SAID, M.B., B.S. (Pb.), D.P.H. (Edin.),
D.T.M. (L'pool), T.D.D. (Wales)
CAPTAIN, I.M.S.

WHILE exploring the possibility of culex production in septic tanks, an interesting observation has been made of the ability of *Chrysomya megacephala* to breed continuously in the fermenting faecal material, in a closed space.

The septic tanks in question (figure 1) are masonry structures with a cubic capacity of 2.5 cubic feet to 3.0 cubic feet per user. They are divided by 2 masonry walls into 3 compartments. In compartments (a) and (b), the fermentation

to open the manholes and make dips for the culex in compartment (c) and search for the larval stages of *Chrysomya megacephala* in the scum, in compartments (a) and (b), where alone the larvæ could have pupated. A pure culture of *Culex fatigans* was obtained and muscoid puparia, presumably those of *Chrysomya megacephala*, were found in the dry scum.

As a control measure, the cowl was removed (figure 3), the top end of the soil pipe covered with mosquito-proof muslin cloth and the cowl replaced (figure 4). *Culex* production stopped in a week, but the breeding of chrysomyia continued even after the access to the tank from the outside was eliminated, adults still being found for 18 weeks in the septic tanks. after sealing.

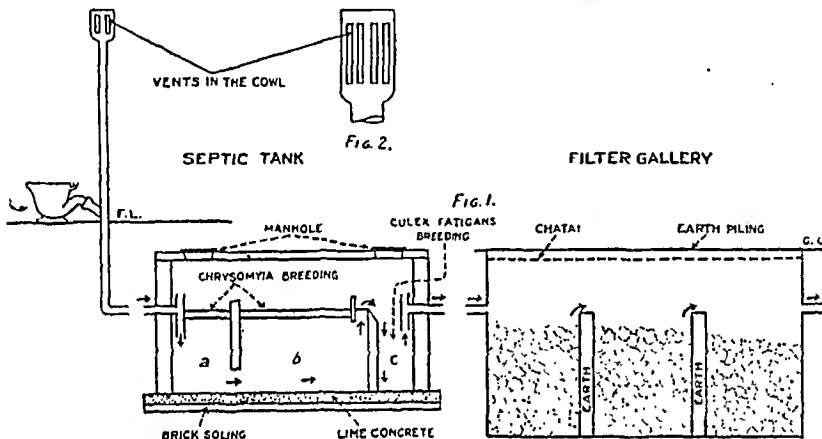


Fig. 1.—Water closet, soil pipe, sewer, septic tank and filter gallery.
Fig. 2.—Cowl with 12 slots (or vents)—each 9 inches by $\frac{1}{4}$ inch.

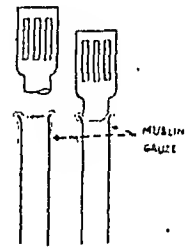


Fig. 3.—Cowl separated and top end of soil pipe covered with muslin cloth.
Fig. 4.—Cowl replaced.

takes place. A solid scum of 6 inches to 9 inches depth forms on the surface under which the anaerobic digestion takes place under ideal conditions. It is here in these two compartments that chrysomyia breeds.

In compartment (c), most of the faecal material has liquefied. No scum forms on the surface. Here *Culex fatigans* breeds.

The digestion is completed in the filter gallery which consists of 3 compartments again, divided by means of 2 earth partitions. The whole structure is non-masonry, being just a large excavated pit in the ground with a capacity of 10.0 cubic feet per user. This is filled up with brickbats and works more or less on the principle of the soakage-pit.

The first step in the investigation was to fix a mosquito-trap on the top end of the soil pipe including the cowl (figure 2), because the vents (slots) in the cowl were the only inlets and outlets through which the culex could go in and out of the septic tanks. This was tied at dusk to eliminate the possibility of collecting day-resting mosquitoes. A large number of *Culex fatigans* and *Chrysomya megacephala* were caught in the trap. These could only have come from the inside of the septic tanks. The trap was kept tied for 5 days and every morning fresh specimens were collected. The next step was

The latter finding, viz, the continued breeding of chrysomyia in such a situation appears quite a new observation.

I am highly indebted to Major R. Senior White, F.R.S.E., malariologist, B. N. Ry., for identifying *Chrysomya megacephala* and for his valuable suggestions.

A Mirror of Hospital Practice

A CASE OF BENIGN NEUTROPENIA TREATED BY SODIUM PENTNUCLEOTIDE

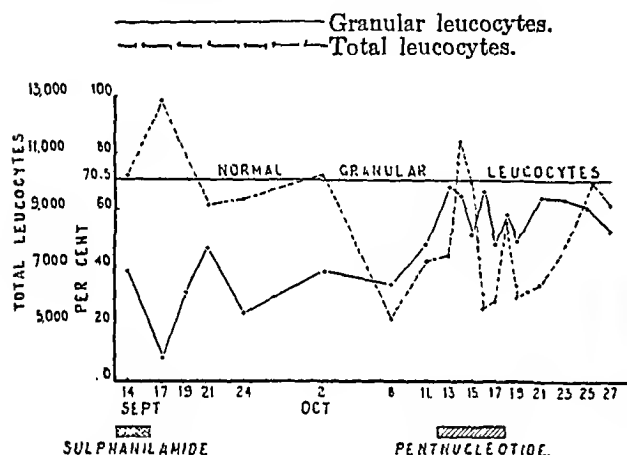
By S. McDONALD, M.D.
MAJOR, R.A.M.C.

Pathologist at a Military Hospital

THE patient, J. D., a soldier, aged 26, was admitted into hospital on 13th September, 1941, suffering from acute follicular tonsillitis of three days' duration. Five weeks previously he had undergone sub-mucous resection of the nasal septum, from which operation he had made a good recovery. He was flushed and restless with a temperature of 101.5°F. The tonsils were grossly enlarged and showed a marked follicular septic exudate associated with cervical adenitis. A throat

swab showed β -hemolytic streptococcus in almost pure culture. He received an initial dose of sulphanilamide grammes 2, followed by a similar dose in four hours and gramme 1 at four hourly intervals. The temperature became normal by 15th September and treatment was discontinued on the following day, after the patient had received grammes 20 of sulphanilamide. Notwithstanding a rapid clinical improvement, his leucocyte picture up to 11th October showed persistent neutropenia though the total count varied little from the normal (*see figure*).

The leucocyte count on 14th September was as follows: total leucocytes 10,200; polymorphonuclears 2,907, band form 918, meta-myelocytes 153, myelocytes nil; eosinophil nil; basophil nil; lymphocytes 5,100; and monocytes 1,122 per c.mm. Thereafter the count was repeated eighteen times; the total count varied from 9,200 to 12,800, and polymorphonuclears from 704 to 6,441 per c.mm. A number of myelocytes were seen twice. The last count done on 27th October showed total white cells 9,200; polymorphonuclears 4,186; band form 276, meta-myelocytes nil, myelocytes nil, eosinophils 322; basophils 92; lymphocytes 3,312 and monocytes 1,012 per c.mm. The mean total neutrophils per c.mm. (a) before, (b) during, and (c) after pentnucleotide therapy were $2,777 \pm 377$, $4,648 \pm 702$ and $4,293 \pm 161$ respectively.



Pentnucleotide therapy was instituted on 12th October. He received 10 c.cm. twice daily until 15th October, and then 10 c.cm. once daily until a total of 100 c.cm. had been given. The patient was transferred to a convalescent depot on 28th October and was discharged to full duty on 14th November, 1941.

Discussion

While the typical appearances of agranulocytic angina were not presented in this case, the question of a possible relationship between sulphanilamide therapy and the neutropenia requires consideration. The patient received only grammes 7 of sulphanilamide during the sixteen hours which preceded the first blood count on 14th September, and it seems likely that neutropenia must have existed before treatment was commenced. Sixteen hours after treatment had been discontinued his total granulocytes amounted to 8.5 per cent but at this time the total leucocyte count was 12,800 per c.mm. In view of these figures there is nothing to implicate sulphanilamide as a factor in causing or maintaining the neutropenia.

The blood picture in this case represents an atypical reaction to pyogenic infection in that neutropenia with a non-regenerative left shift

and absolute lymphocytosis occurred at an early stage of the infection. Similar pictures in the convalescent phase of pyogenic infections were recorded by McDonald (1931) but the lymphocytosis in this case is clearly not of the usual post-infective type. On the whole, the appearances suggest that a constitutional neutropenia existed and that this condition may have been aggravated by pyogenic infection.

The use of pentnucleotide constitutes an attempt to assess the value of the drug in benign neutropenic conditions. Case reports by Hall (1934), Ranson (1935), Fettes and Whitby (1935) and Castleden (1935) have cast doubt on the ability of pentnucleotide to avert a fatal issue in agranulocytic angina but Grenet *et al.* (1939) have recorded a successful case. In this communication it is stated that in certain cases of benign subacute neutropenia pentnucleotide has caused a return to the normal leucocyte picture.

Leucocyte counts in the case under discussion have been subjected to statistical analysis. Figures for total neutrophils (segment-nuclear + band form + meta-myelocyte + myelocyte) have been grouped as (a) before, (b) during, and (c) after pentnucleotide therapy. The greatest difficulty in assessing the significance of the differences of the means of these groups is presented by the relatively large variance in group (b). As a result, application of the 't' test to the significance of the difference between the means of groups (a) and (b) gives the answer that there is one chance in about eighty of getting a second random sample of data of the same size as group (a) and from the same population in which the mean is as high as that observed for group (b). That is, there is considerable probability that the data of group (b) are drawn from a different population from those of group (a) indicating that pentnucleotide has significantly altered the level of the total neutrophils. There is no significant difference between the means of group (b) and group (c).

It may therefore be justifiably concluded that the neutrophil count was significantly higher during and after pentnucleotide therapy but data derived from the treatment of a single case must be accepted with caution.

I am indebted to Colonel H. F. Humphreys, late R.A.M.C., for permission to publish this case, and to Dr. R. B. Fisher, department of biochemistry, Oxford University, for the statistical analysis.

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FOREIGN BODY IN THE ŒSOPHAGUS: REPORT OF THREE CASES

By JAGDISH SINGH, M.B., B.S., F.R.C.S.E.,
F.R.C.S. (Eng.)

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CASES of foreign body in the Œsophagus are usually seen in children. The cases reported were seen in adults, and sought treatment within a few days of each other.

Case 1.—A Sahnsi male (Sahnsies belong to the criminal tribes in the Punjab), aged 40, arrived at the hospital with the complaint of difficulty in swallowing, and swelling of the neck. Both these complaints started 8 days ago when he was taking cooked meat. His own statement was that a piece of bone was stuck in his Œsophagus. Local examination showed a hard brawny swelling of the root of the neck more marked on the left side. His pulse was 120 per minute and his temperature 101.4°F. A provisional diagnosis of a piece of bone in the Œsophagus with cellulitis of the neck was made. X-ray examination revealed the shadow of a piece of bone about 1½ inches long projecting in the region of the Œsophagus opposite the upper part of the body of first thoracic vertebra. Because of the presence of cellulitis, it was decided to remove the piece of bone by Œsophagotomy.

The operation was performed under intravenous cyclonal sodium anaesthesia. A transverse incision 2 inches long was made on the left side of the root of the neck. On dividing the deep fascia a good deal of foul smelling pus escaped. Examination with the gloved finger revealed an abscess by the side of the Œsophagus. The abscess was opened by the finger being pushed in. On further search the end of a piece of bone was felt, and it was removed with a pair of forceps.

Progress of the case.—On account of the presence of cellulitis the patient was given 4 grammes of sulphanilamide daily for 4 days. He began to make progress but there was some leakage of fluid from the operation wound for a fortnight. The case was discharged completely cured on the 24th post-operation day, i.e., 10 days after the closure of the Œsophageal fistula.

Case 2.—A Sikh married woman of 26 years was admitted with the complaint of inability to swallow anything. This complaint started 24 hours previously when she was swallowing a partly chewed nutmeg. Indirect laryngoscopic examination did not reveal any nutmeg. She was, therefore, examined under the x-ray screen during a barium swallow. She swallowed the barium meal with difficulty but nothing abnormal was seen. After the examination, however, she felt completely relieved except for stomatitis. She was discharged cured the next day.

Case 3.—A Sikh married woman of 19 was admitted 2 days after the discharge of case 2 with the following history:—

In the morning she was swallowing partly chewed nutmeg when she felt suddenly choked and thought she was going to die. She was removed to the hospital by her husband immediately.

The condition of the patient appeared serious, her pulse and respiration were, however, normal. Indirect laryngoscopic examination did not reveal the presence of a foreign body. On account of the frequent fits of choking, she could not swallow the barium meal and the presence or absence of a nutmeg in the Œsophagus could not be settled by x-ray examination.

She was, therefore, examined by passing an Œsophageal speculum which showed the presence of a piece of nutmeg impacted at the Œsophageal opening. As the patient felt very uncomfortable the Œsophageal speculum was removed and she was given intravenous cyclonal sodium anaesthesia. The Œsophageal speculum was passed and a piece of nutmeg which was impacted

at the opening of the Œsophagus was removed. The Œsophagus was examined by passing an adult size Œsophagoscope and another piece of nutmeg was removed from about the middle of the Œsophagus. The two pieces joined together made almost a whole nutmeg. Afterwards she had no difficulty in swallowing, her only complaint being some stomatitis. She was discharged completely cured after 2 days.

Summary

Three cases of foreign body in the Œsophagus in adults have been reported.

A CASE OF ACUTE CUTANEOUS GLANDERS IN MAN

By G. PANJA, M.B. (Cal.), D.Bact. (Lond.)
*Officiating Professor of Bacteriology and Pathology
and*

B. C. CHATTERJEE, M.B., D.T.M., D.P.H.
*Lecturer on Infectious Diseases, School of Tropical
Medicine, Calcutta*

GLANDERS in man is rare in India. The Principal of the Bengal Veterinary College has reported that the disease is extremely rare here in man. Mr. Rajagopalram of the Imperial Veterinary Research Institute, Mukteswar, Kumaun, wrote to one (G. P.) of the authors of this note that he knew of only two cases of glanders in man in this country, both being veterinarians—Professor Gaiger (1913, 1916) and Mr. Shilston. Up till now no acute cases of cutaneous glanders have been reported in India. It is partly for this reason and partly because of resemblance of this case to variola that we are making this report. In fact, the case would have been diagnosed as smallpox if a bacteriological investigation had not been made. Professor Gaiger suffered from chronic glanders of bones and joints with acute exacerbations. He suffered for 28 months, having undergone 45 operations. Mr. Shilston suffered from acute pulmonary glanders. Two cases in members of the staff of the Bengal Veterinary College are doubtful, as no bacilli were isolated. Our case was thoroughly investigated by one of us (G. P.) from the bacteriological point of view. The report is as follows:—

Alauddin, a healthy Mohammedan male, aged about 30, was admitted as a case of smallpox to the Campbell Hospital, Calcutta. One of us (B. C. C.) doubted if it was a genuine case of smallpox and hence called the other of us (G. P.) to investigate. The patient had an eczematous lesion on the left palm, swollen and tender lymphatics in the forearm leading from the lesion, a big fluctuating abscess above the elbow, and flaccid, pustular lesions without umbilication on the arms, the face and the trunk. High temperature, coated tongue, reddish flush all over the body and marked prostration were present. No enlargement of glands was detected. The patient was semi-conscious and no history could be elicited. He died on the 3rd day after admission.

Cultures from blood, pustules and the abscess were taken during life. No post-mortem examination could be made. Smears of pus showed scanty, Gram-negative rod-shaped organisms apparently capsulated. In the blood culture

fluid, faint turbidity without any hæmolysis was noticed in two days. The same organism was isolated from the blood, the abscess and the pustules. The characters of the organism are described below :—

Culture.—Gram-negative, slender, rod-shaped, some in threads, non-sporing, non-motile (no motility seen in semi-solid agar deep at different temperatures). It forms a mucoid colony in 24 hours, low convex, 1 to 2 mm. in diameter, glistening, with entire margin, easily emulsifiable; in broth, faint turbidity and no pellicle. Growth more mucoid and greyish yellow on glucose agar. Faint café-au-lait on potato in 24 hours. On glycerine agar—white, mucoid growth. Dorset's egg—scanty growth, confluent, showing faint magenta colour. Loeffler's serum—scanty growth. Gelatin 20 per cent—no liquefaction. No hæmolysis on blood agar. On Mac Conkey's



agar after 'five days' cultivation, colourless colony, about 2 mm. in diameter, mucoid and of slight café-au-lait colour. No fermentation of sugars within 18 days. No change in litmus milk, slight alkalinity only after 18 days. Anaerobically—scanty growth. Glucose-agar shake culture—no growth seen except on the top. The organism is therefore aerobic and not micro-aerophilic. Growth slightly improved by CO₂, H₂S not formed; methyl red reaction slightly positive; Voges-Proskauer reaction and Indole negative.

Control tests were at the same time put up with *Pf. mallei* and *Pf. whitmori*, and all the reactions tallied with those given by *Pf. mallei*.

Serological.—A serum raised in rabbits against the organism agglutinated the organism and a

laboratory culture of *Pf. mallei* to full titre (1/6400), but no agglutination was seen with *Pf. whitmori*. Similarly a serum raised against *Pf. mallei* agglutinated *Pf. mallei* and the organism isolated to full titre (1/3200). Cross-absorption tests showed that both the organisms were serologically identical.

Complement-fixation tests with mallein and both the sera were equally positive, the one raised against the organism and the other against *Pf. mallei*.

Pathogenicity.—A male guinea-pig was injected intraperitoneally with 0.5 c.cm. of a one-day-old broth-culture. It died in two days. P.M.—Congestion in lungs, slight sanious exudate in pleura and peritoneum. Smears from exudate showed Gram-negative, capsulated bacilli. Cultures from peritoneum and heart's blood showed the same organism. A male guinea-pig injected with 0.1 c.cm. of the culture died in eight days with swollen testes (positive Straus reaction), nodules in the peritoneum, and positive blood culture. A dermal inoculation by scarification killed the animal in 21 days; there were inflamed vesicles at the site of inoculation; nodules in liver and spleen and blood culture positive. A guinea-pig fed orally with 1 c.cm. of the culture died in 10 days showing a positive Straus reaction. Rabbits injected subcutaneously and cutaneously showed ulceration at the sites of inoculation and died in 19 days. A monkey injected subcutaneously with 0.2 c.cm. of the culture died in five days showing ulceration at the site of inoculation, ulcers in eyes with purulent discharge, and marked emaciation; at post-mortem no naked eye changes were seen in internal organs but blood culture was positive. All these animal experiments were undertaken as soon as the organism was isolated and before it was fully identified, so that the organism might not lose its virulence in laboratory subcultures.

Our thanks are due to Dr. B. M. Paul and Dr. N. Dass for helping us in our animal and serological experiments.

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ASCARIASIS SIMULATING ACUTE ABDOMEN

TWO CASE REPORTS

By A. R. SEN, M.B., B.S.

Medical Officer In-Charge, Municipal Hospital,
Amalner, East Khandesh, Bombay Presidency

Case 1.—A boy, aged 10 years, was admitted on 5th September, 1941, at 6 p.m. for the following complaints :—

1. Sudden pain in the right side of lower abdomen for six hours.
2. Vomiting and nausea for four to five hours.

History.—The pain started at about 12 noon; it was almost constant, and localized in the right iliac fossa. He had vomited three or four times.

Examination.—Pulse—110, respiration—24 per minute. Temperature—100.2°F. Tongue—slightly coated and moist. The patient was looking acutely ill. There was acute tenderness over the McBurney's area, and a small lump about the size of an egg was felt in the right iliac fossa. There was little rigidity of the abdominal wall. Hyperæsthesia in Sherrin's triangle was present. White cells—10,670 per c.mm.

Provisional diagnosis.—Acute appendicitis.

Treatment.—The patient was put on Ochsner-Sherren treatment. At about mid-night he vomited a round worm, and slept for the rest of the night. Next morning, he was given carbon tetrachloride and oil of chenopodium in two divided doses at an interval of an hour, followed by a dose of castor oil after two hours. He passed altogether ten round worms. The lump in the right iliac fossa completely disappeared and the patient recovered.

Case 2.—A Mohammedan female, aged 18 years, was admitted on 10th February, 1941, for the following complaints:—

1. Acute pain in the right side of the abdomen for four days.

2. Jaundice and repeated vomiting for two days.

There was a history of a similar attack of acute pain in the right hypochondrium about six months before. The pain was colicky in nature, but did not radiate to the back. Stools were clay-coloured.

Examination.—Pulse—100, respiration—20 per minute. Temperature—99.8°F. Tongue—moderately coated and dry. Conjunctiva and back of the tongue were tinged yellow. Pain and tenderness in the right hypochondrium were present. Murphy's sign was positive.

Rectal examination.—Nothing particular. White cell—8,760 per c.mm.

A provisional diagnosis of acute cholecystitis (gall-stone?) was made and she was treated accordingly. On the following day her condition slightly improved. In the evening she vomited two round worms. Next morning, carbon tetrachloride with oil of chenopodium was given in divided doses followed by an ounce of saturated solution of magnesium sulphate. About 8 or 9 round worms were passed with stools. She felt much relieved. Jaundice disappeared completely. Afterwards she had an uneventful recovery.

Points of interest.—It is probable that the local lump in case 1 was produced by aggregation of round worms in the cæcum while jaundice and colicky pain in case 2 were due to their blocking the ampulla of Vater. The possibility of worm infection should be borne in mind in a suspected case of acute abdomen, especially in children.

A CASE OF CONGENITAL ABSENCE OF THE PENIS

By K. M. LAL, M.B., B.S., P.M.S.

Medical Officer In-Charge, Sadar Hospital, Gorakhpur

S. L., aged 50 years, came to this hospital because of difficulty in micturition.

On examination it was found that the penis was completely absent and that there was a small raised portion of skin at the site of the root of the penis. The urethral opening was in the middle of the perineum, about an inch in front of the anal orifice. The testicles were developed and hydrocele was present on both sides. The

secondary male sexual characters were all present (figures 1 and 2).

The patient stated that the penis had been totally absent since birth, and that he had had no difficulty in passing urine through the urethral opening. Only recently had he felt some obstruction.



Fig. 1.

The urethral opening was cleaned and the passage easily dilated up to 9/12. The patient passed urine quite freely, and has not attended since.



Fig. 2.

The case is interesting from several points of view: (1) the congenital absence of the penis only, (2) the presence of the other secondary male sexual characters, (3) the presence of hydrocele, and (4) the age at which the patient first reported for medical advice.

PROGRESS IN SULPHANILAMIDE THERAPY

It is now generally agreed that the therapeutic value of sulphanilamide compounds far out-weighs the side reactions often manifested, if proper choice be made on the drug that is to be used in any particular infection. A more tolerated drug is an improvement over a more acute drug in any sulphanilamide therapy. Any small difference in antibacterial action can be easily adjusted in the case of a more non-toxic but an effective drug by the administration of appropriate dosage.

So many products are now available that clinicians are at a loss to distinguish the advantage of one over the other in any particular bacterial infection. In meningitis, *B. coli*, and in streptococcal infections cheaper and simple drug containing only sulphanilamide is usually the drug of choice. This is marketed in the form of tablets and as such contains many other substances other than pure sulphanilamide. The adjuvants must be those substances which would again mitigate the side effects of sulphanilamide such as acidosis, dizziness, etc., and the whole tablet should disintegrate rapidly so that the drug may be easily absorbed in the system. Further this being a drug of aniline group¹, should not be unnecessarily stored as this storage often increases the toxicity of drug and, as such, a freshly prepared tablet should always be preferred. In all these respects Bi-Sulphonamide would be found to be the drug of choice. Being freshly prepared with suitable adjuvants from purest brand of *p*-amino benzene sulphonamide it creates wonders in patients suffering from all types of streptococcal infections. Whenever the patient cannot tolerate or swallow the drug by mouth, or when the conditions of the patient do not allow a proper concentration of the drug in the blood then the question of parenteral administration arises. But as sulphanilamide is not so soluble in water it will have to be converted to other soluble derivatives and it is for these reasons that the physicians find various soluble derivatives again in the market. Mostly are some sodium derivatives—some are coloured and some are colourless. In cerebrospinal infections the red colour variety penetrates from the blood to theca more slowly than sulphanilamide². In urinary infections the excreted product is only a urinary antiseptic in so far as the compound has been reduced to colourless sulphanilamide. In urgency the coloured variety cannot be injected intravenously. On the other hand in Bi-Sulphonamide (Injection) a soluble derivative of sulphanilamide would be found which is well tolerated, may be introduced subcutaneously, intramuscularly and even intravenously. It is rapidly absorbed and easily eliminated with the liberation of sulphanilamide through the urine. As such Bi-Sulphonamide (Injection) is invariably being found to be clinically more effective in streptococcal and meningococcal infections including influenzal meningitis³. There are certain mixed infections when a synergy treatment with vaccine would offer a better clinical result,^{4,5,6} particularly in staphylococcal and pneumococcal (type III) infections.

The extensive investigations carried out for finding out the mechanism of the sulphanilamide therapy⁷, have afforded to the physicians a number of substances for combating not only against Gram-positive bacteria but also against other types like gonorrhœa, *B. coli*, etc. But in selecting drugs for gonococcal infections, a caution is necessary. People of low vitality suffer from various physiological disorders and sulphanilamide drugs are now being found to cause even circulatory disturbances. A well tolerated and less toxic drug should be again of choice. In Bi-Anicide the clinicians would find the armament necessary for combating against gonococcal and other infections of the urinary tract^{8,10}. In emergency a soluble derivative⁹ of Bi-Anicide would always be available to help in ameliorating the conditions of the suffering public.

Knowledge begets knowledge. It is now being observed that a 2.5 per cent solution of Bi-Anicide is a good remedy against conjunctivitis, gonococcal ophthalmia and other eye infections. It is slowly absorbed through the lachrymal fluid and exerts no side reaction. All the above products—Bi-Sulphonamide (Tablet), Bi-Sulphonamide (Injection), Bi-Anicide (Tablet), Bi-Anicide (Injection)—are being manufactured and issued by Bengal Immunity Co., Ltd., always in standard and potent conditions to combat against the bacterial infections in the tropics.

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Indian Medical Gazette

MARCH

HEPATITIS, SPORADIC AND EPIDEMIC

HEPATITIS frequently results from infection through the portal circulation secondary to amoebic ulcers in the intestine, or to some intra-abdominal inflammatory condition. It may be caused by systemic blood infection; for instance it contributes to the clinical picture of spirochaetosis ictero-haemorrhagica, yellow fever and malaria, and of septicæmic states. It may also be due to ascending infection of the biliary tract. Autogenous toxins may be responsible in some cases, as in the toxæmia of pregnancy, and the so-called acute yellow atrophy. Among the poisons which damage the liver cells are arsenic, chloroform, carbon tetrachloride, trinitrotoluene, tetrachlorethane, phosphorus, gold, cinchophen products, and mushroom poison.

Apart from these well recognized causes, epidemic outbreaks of hepatitis, frequently with jaundice, have been reported from time to time, and variously designated as 'jaundice of camps', 'jaundice of campaigns', 'infective or epidemic hepatitis', 'epidemic catarrhal jaundice', etc. There were over 2,000 cases of epidemic hepatitis among British troops in Mesopotamia during the last war. Widespread outbreaks of non-spirochaetal acute hepatitis were reported in Sweden in 1926-27. Cases have been encountered in several places in England. Recently, jaundice occurred in epidemic form among troops in India, Africa and the Middle East.

The exact aetiology of this disease is still obscure. It is usually regarded as being due to a virus infection. It has been known to follow a blood transfusion, the infection being transmitted directly from an abortive attack of the disease in a blood donor without icteric manifestations. It may also result from the therapeutic use of human serum—commonly pooled immune serum. A number of cases have been attributed to inoculation with certain lots of yellow fever vaccine after a period varying from a few weeks to a few months. It has been shown that these cases were not caused by the yellow fever virus, but probably by an infective agent present in the particular lot of human serum used for suspending the virus, and that the agent was carried in the tissue culture used for growing the virus.

The usual mode of infection is not known. All the evidence points to direct spread from case to case. The possibility of animal vectors has been considered, and it has been suggested that this infective condition in man is acquired through the alimentary tract, possibly from diseased animals. In this connection, Anderson and Tulinius made interesting observations.

They succeeded in causing jaundice and hepatic changes in healthy pigs by feeding them with the liver from pigs suffering from porcine hepatitis, and also with duodenal juice withdrawn from patients suffering from epidemic jaundice.

Pathological lesions are characterized by necrosis of the parenchymatous cells of the liver, especially in the central parts of the lobules. Repair occurs by multiplication and hypertrophy of the healthy liver cells. Destruction of the liver tissue is invariably accompanied by a mild inflammatory reaction. Hence the term 'infective hepatitis' is proper since it signifies the infective as well as the inflammatory nature of the condition.

The mode of spread not being clearly known, it is not possible to determine the exact incubation period. Most observers consider it to be from 3 to 6 weeks. The clinical picture resembles closely that of catarrhal jaundice caused by acute gastro-duodenitis and temporary blocking of the common bile duct. In this condition the initial catarrhal symptoms are prominent; the patient usually complains of nausea, vomiting, anorexia, upper quadrant discomfort and rise of temperature. In two or three days these symptoms subside, while jaundice develops. The gall-bladder may be palpable when the patient is jaundiced. In acute infective hepatitis however there are no pre-icteric symptoms. Mild constitutional symptoms such as lassitude, headache, pain in the body, and fever are the chief early symptoms, followed by the appearance of jaundice. The urine becomes dark but the stools are normal-coloured, bile being invariably present. The liver is slightly enlarged and tender, and the spleen is often palpable. The symptoms are obviously not specific enough to differentiate the condition, and diagnosis is difficult except in times when other cases are also prevalent. The presence of bile in the stool, fever and frequent enlargement of the spleen are however important features of this disease. Most cases usually run a mild course and recover completely in a month or two. There may be cases without jaundice. Occasionally severe cases are encountered; the patient becomes increasingly toxic and dies of hepatic necrosis.

The white cell count is usually within normal limits. The blood and urine contain bile pigment. A prompt direct van den Bergh reaction in true catarrhal (obstructive) jaundice and a biphasic reaction in cases of mild infective hepatitis are usually obtained, but this fact is of little value in distinguishing between the two. The lævulose-tolerance test in catarrhal jaundice ordinarily shows no hepatic insufficiency, whereas in infective hepatitis, this is well marked from the onset of illness. This fact may be of considerable help in differential diagnosis. This however is a laboratory finding and laboratory facilities may be lacking. The chief clinical point in differ-

ential diagnosis is the colour of the stool, fairly normal in infective hepatitis with the presence of bile, and pale in catarrhal jaundice with the reduction or absence of bile.

It should be remembered that infective hepatitis is by no means a rare disease in this country. It is only by a more careful study of cases of jaundice, that the frequency of this condition can be determined with accuracy; by such a study the clinical differentiation of infective

jaundice from catarrhal jaundice may be rendered easier.

R.N.C.

CORRIGENDUM

Major Andreassen, I.M.S., writes that in his article 'Notes on the Use of Cotton in Surgery, and on Plaster Technique' published in the December 1942 issue (page 712), the statement made that '3,000 cases of intestinal obstruction were admitted yearly' (*vide* page 713, column 1, para 3, line 6) is incorrect. The correct figure is 300. The error was in the manuscript.—
EDITOR, I. M. G.

Medical News

PRODUCTION OF DRIED BLOOD SERUM IN INDIA : POST-WAR IMPORTANCE OF TRANSFUSION SERVICE

It is understood that one of the desiccating machines for the drying of blood ordered by the Government of India from America has reached India and has been set up at the All-India Institute of Hygiene and Public Health, Calcutta, where the production of dried serum is now being undertaken. The second machine when it arrives will be installed in the Haffkine Institute at Bombay.

With these two machines, over 100 pints of the dried product can be produced every week. Preliminary experiments have shown that the dried material can



Plant for drying blood plasma or serum together with prefreezing unit, built by the All-India Institute of Hygiene and Public Health, Calcutta.

readily be manufactured in India and, provided that sufficient donors come forward, there is nothing to delay production on a fairly large scale as soon as both the desiccating machines are in full working.

Lest there should be a tendency in some quarters to take the view that, with the improvement in the general military situation, the need for an adequate supply of fresh blood will be reduced, it should be stressed that the blood transfusion service now being organized for India will still be of vital importance to the civil population after the last shot has been fired in this war. A blood transfusion service should be regarded as part of the normal peace-time medical facilities provided in our civil hospitals. The service is being developed on that basis, and any lessening of the chances of invasion cannot have the slightest effect in reducing the need for blood donors wherever blood banks have been started.

IMPLANTING HORMONES

THE body contains elaborate systems of control, which enable it to operate in an appropriate way. One of

these is the network of nerves, which co-ordinate actions by means of electrical messages, like the currents in a telephone system. Another is a system of glands, which discharge active substances into the blood stream. These substances are named hormones, and are carried by the blood to the organs which respond to them. The hormones may be regarded as chemical messengers which tell the organs what to do. If a gland producing a hormone is deficient, or becomes diseased and is removed, the organ controlled by the hormone can no longer act properly. It may be necessary to replace the hormone which would normally have come from the gland by artificial administration from outside.

The usual procedure is to inject a solution either into a muscle or under the skin, from whence the substance is absorbed into the circulating blood. Absorption, however, is usually rapid and even where injections are made daily, the supply to the responding organ tends to be irregular, being greatest, perhaps even excessive, shortly after injection, and least, perhaps altogether deficient, just before injection. This irregularity leads to great inefficiency.

Some years ago Dr. Ruth Deanesly and Dr. A. S. Parkes, of the National Institute for Medical Research in London, discovered that the female and male sex hormones, oestrone and testosterone can be administered in the form of a compressed tablet or pellet of the pure crystalline substance implanted beneath the skin. Under these conditions, absorption is extremely slow and very high effectiveness is obtained, since the wasteful irregularity in the supply to the responding organ is avoided. The technique has the further advantage of eliminating repeated injections. At any desired time after implantation, the tablets can be removed, cleaned, dried, and re-weighed, and the amount absorbed determined. The technique has now been extended successfully to several other active substances, including progesterone, from the corpus luteum, desoxycorticosterone, from the adrenal cortex, and the synthetic substances which have biological activity similar to that of oestrone. Preliminary experiments have also been carried out with adrenaline, thyroxine, and insulin.

INDIAN MEDICAL COUNCIL

COLONEL P. B. BHARUCHA, D.S.O., O.B.E., V.H.S., I.M.S., Member of the Faculty of Medicine, Punjab University, has been duly elected to be a Member of the Medical Council of India under clause (b) of sub-section (1) of section 3 of the Indian Medical Council Act, 1933 (XXVII of 1933), with effect from the 7th December, 1942.

PROPHYLAXIS OF ASTHMATIC ATTACKS



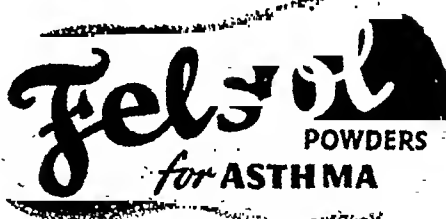
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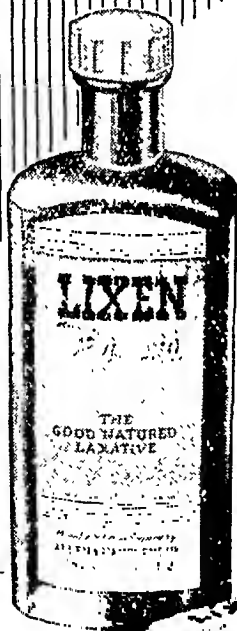
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Public Health Section

DESIRABLE MINIMUM FUNCTIONS AND ORGANIZATION—PRINCIPLES FOR HEALTH ACTIVITIES

AN OFFICIAL DECLARATION OF THE AMERICAN PUBLIC HEALTH ASSOCIATION ADOPTED 9TH OCTOBER, 1940*.

As a result of 75 years of practical experience, the basic principles of official health services are now everywhere recognized as necessary in any community of modern society. These principles have been accepted generally by the governments of the United States and Canada, and are universally endorsed by the several professions concerned. The protection and promotion of the health and welfare of the citizens are conceded by all authorities on political science to be essential functions of government and to be duties inherent in the modern state, although the obligation may be delegated in large part to its political subdivisions.

With these considerations in mind, the following general policies may be stated:—

1. A health problem becomes one of public concern when, because of its nature and extent, its solution requires organized group action.

2. A community is responsible for those public health procedures that are community-wide in their application (as in the case of sanitary measures) and for those that are intended to conserve the health of individuals who, for any reason, are unable to command health protection at their own expense.

3. Public health service may properly include not only well-recognized procedures, such as those of sanitation, vital statistics, the prevention and control of communicable diseases, and health education of individuals, but also:

(a) Needed services, unless otherwise provided, for individuals afflicted with certain conditions and diseases which have a wide prevalence, a high cost of treatment, and are amenable to organized effort, such as those already found practicable in the treatment under public auspices of mental disease, tuberculosis, cancer, pneumonia, and syphilis.

(b) Such responsibility for other medical care of individuals as may be delegated by legislatively expressed public policy to the health department rather than to some other branch of government.

Responsibility in regard to care of the sick

Various forms of tax-supported medical care are in operation for needy persons in many communities by the action of local or state government. These systems are expanding. Many professional societies and lay organizations are also undertaking plans for the provision of medical care on a prepayment or insurance basis for self-supporting persons of small means.

Included among the obligations of the medical officer of health to the community is that he inform himself as to the facilities for the general care of the sick, their character and distribution,

and that he make use of his position to see to it that any important inadequacies are corrected by appropriate action.

We believe that health officers should participate with other governmental and with voluntary bodies, particularly the medical profession, in planning for the improvement, co-ordination, and extension of medical facilities and services. Diagnostic facilities, treatment, and individual instruction in personal hygiene, through medical conferences and visits by public health nurses, should be provided by health departments for all persons needing such services who are not in position to obtain them under conditions which make their general utilization reasonably probable.

Essential local public health services

A modest but adequate health programme can be guaranteed if the following basic principles of work are observed.

For all official health organizations operated under federal, state, or local authority, leadership and responsibility should be vested in a full-time trained health officer appointed on professional qualifications and secure against political interference or dismissal during competent performance; he should receive a salary equivalent to the net income of physicians or other professional men of equal training, and commensurate with the public responsibilities placed upon him; he should not engage in any other gainful occupation inconsistent with the proper conduct of his office, such as the private practice of medicine, and should be required to give his whole time to its duties; annual appropriation for official health work totalling at least \$1.00 *per capita* of population served should be provided for the minimum activities hereafter described, and exclusive of medical care and hospital services; freedom for the health officer to select trained personnel for medical, nursing, sanitary, laboratory, and statistical activities from lists of persons of proved competence should be assured.

There should be in every state (or province) or city, a board of health or public health council (serving preferably without pay). The function of such a board of health or council should be to advise with the health officer in determining the general policies of the health department and to enact those ordinances or regulations for which it has authority. The same principle is probably applicable in smaller local units, counties, or rural health districts. Such a board should have no administrative or executive functions.

This body should include physicians, members of other appropriate professions, and representatives of the general public.

The state, city, or other local health officer should be directly responsible either to his board

* Extract from *American Public Health Association Year Book*, 1940-41, p. 43.

of health, or to the chief executive of the governmental area concerned.

With such leadership and resources, a programme of local health department activities should be undertaken which will include at least the following six primary functions of modern health departments and should be directed by full-time trained experts responsible to the health officer, except where the organization is too small to justify such desirable specialization of personnel.

Local health department functions

A. Vital statistics.—The collection, tabulation, analysis, interpretation, and publication of reports of births, deaths, and notifiable disease. This, the first public function upon which all competent planning for health protection is based, is no more than the official book-keeping of the human family within the political or governmental unit.

B. Sanitation.—The control of the material environment of man in the interest of human survival, comfort, and use.

The specific responsibilities in this respect include :—

1. Safeguarding all water supplies, both public and private, commercial and household, so that the purity of the water for dietary, cleansing, or recreational use may be universal.

2. Securing the sanitary disposal of human and industrial wastes in a manner to avoid nuisance, and prevent the pollution of foods or water supply.

3. Supervision of the production and distribution of milk, and milk products, by licensing, inspection, and laboratory tests, to prevent the sale of any but a clean, wholesome pasteurized milk of standard food value.

4. Supervision of the production, processing, and distribution of foodstuffs, including shellfish, and of drugs and devices offered to the public for treatment of sickness.

5. Supervision of all places of human habitation to secure adequate light, air, water, sanitary necessities, protection from inclemencies of weather, and to prevent overcrowding of occupants. Also control over the environmental sanitation of public camp sites, swimming pools, bathing beaches, parks, and other public properties. (Present community housing programmes offer the health department opportunity for co-operative leadership.)

6. Control of mosquitoes, other insects, rats and other vermin, such as may affect the public health.

7. Control over the environmental conditions of employment.

8. Control over atmospheric pollution by smoke, dust, and harmful fumes.

C. Control of communicable and preventable diseases.—Disease control has always been and continues to be a basic activity of public health service. Health departments will fail to win the confidence of the general public or will fall in public esteem if they do not succeed in preventing epidemics of certain communicable diseases. Practical application still lags far behind definite knowledge already attained which would enable physicians, public health authorities, and an enlightened public, working intelligently together, to make much greater progress in the control of many communicable diseases and to eradicate others as public health problems.

Specific responsibilities of the health departments include provision for the reporting of cases, the isolation of patients, and immunization of susceptible persons.

With regard to tuberculosis, syphilis, gonorrhœa, malaria, hookworm disease, and epidemic diarrhœas, there must be also systematic effort to find cases of infection not yet the subject of official report. Diagnostic, consultative, and treatment facilities must be provided where necessary, and particularly for tuberculosis, there is needed x-ray service for diagnosis and review of progress, and sanatorium care.

Health department service for other than communicable diseases of preventable character and of public health interest should include studies of incidence, diagnostic service, and educational activities.

D. Laboratory services.—A well-organized public health laboratory with a competent professional staff is one of the fundamentals of effective health work with the communicable diseases, and is useful to an increasing degree in a wide variety of correlated public health functions.

Specific responsibilities of health departments include the building up and maintaining of a laboratory service which will provide assistance to practising physicians and the department's staff in the diagnosis of communicable disease. A prompt and reliable laboratory service will be an important factor in stimulating friendly relations between physicians and the health department. Control of foods and many other features of general sanitation depend for their effectiveness upon the skills and technics of the public health laboratory.

E. Protection of health in maternity, infancy, and childhood.—Beginning its social concern with the health status of the man and woman preparing for marriage, continuing with the protection of the health of the expectant mother, the new-born, the infant, the pre-school and school child, and finally supervising the conditions of work and the fitness to work of young people, the health department deals with the important problems of human reproduction, growth, and development. Efficient conduct of services for the safeguarding of the health of mothers and young children materially reduces the burden of activities intended to control tuberculosis, syphilis, and other communicable diseases, and lessen the load placed on the school health service. Such functions are interrelated and must be co-ordinated.

Whether school health service is provided by the department of health or by the educational authorities of the community, there should be formal provision for collaboration between these two departments of civil government (the schools and the health agencies) to avoid duplication of services and conflict of authority.

F. Public health education.—Modern public health practice has shown how to prevent much sickness and many premature deaths. It is a

responsibility of health departments to make the knowledge of disease prevention, treatment, and control accessible to the average man in a form that he can understand and make a part of his living. The education of the people in such matters may be accomplished through such channels as newspapers or magazines; the production and distribution of books and pamphlets, pictures and exhibits; by means of personal work with individuals and groups on the part of public health nurses and other professional and lay staff members; by means of lectures, personal and group demonstrations, the film, and the radio.

Many fields of preventive medicine can be cultivated and effective progress made, chiefly or only after the public concerned have learned what they themselves can and must do in their own interest and through the services of their physicians or through community agencies. The campaigns of education against tuberculosis, diphtheria, and syphilis, where official control is of great importance, are instructive examples of what might be achieved in teaching people all the facts they can understand about cancer, diabetes, heart diseases, nutritional diseases, occupational diseases, some diseases of mentality or personality, and especially the care of the expectant mother and of young children. The extent of effectiveness and the limitations of modern medical, sanitary, and related science should be made a part of the knowledge common to all citizens.

Public health nursing

The work of the department of health as it relates to communicable disease control, to maternity and child hygiene, to public health education, and, in many rural areas, to sanitation, depends upon the services of public health nurses professionally directed and supervised.

Public health nurses, qualified to meet the standards of their profession, are essential to effective public health work. In communicable disease control and in giving advice about the feeding, rest, the health of children and mothers, their services are effective and are welcomed. They interpret the directions of the private physicians and of the physician of the health department. Their organizing ability and co-operation can be relied upon for community projects.

Research

Maintenance of essential health services at a high level and assurance of improvement in the critical analysis of all that is done in the public interest require that the personnel of each major division of every health department give time and attention to the review and study of pertinent health problems. The health department should be a source of new and accurate knowledge of preventive medicine and public health practice as well as being the agency through which long established facts of science are made practically effective.

State and national health services

Complementary to the proper activities of local health departments are the health functions of state and national governments.

State health functions include at least the following :—

1. Study of state health problems and planning for their solution as may be necessary.
2. Co-ordination and technical supervision of local health activities.
3. Financial aid to local health departments as required.
4. Enactment of regulations dealing with sanitation, disease control, and public health, which have the force of law throughout the state.
5. Establishment and enforcement of minimum standards of performance of work of health departments, particularly in communities receiving state aid for public health.
6. Maintenance of a central laboratory, and, where necessary, branch laboratories, for the standard functions of diagnostic, sanitary, and chemical examinations; production or procurement of therapeutic and prophylactic preparations, and their free distribution for public health purposes; establishment of standards for the conduct of diagnostic laboratories throughout the state; laboratory research into the causes and means of control of preventable diseases.
7. Collection, tabulation, and publication of vital statistics for each important political or health administrative unit of the state and for the state as a whole.
8. Collection and distribution of information concerning preventable diseases throughout the state.
9. Maintenance of safe quality of water supplies and controlling the character of the disposal of human waste for all communities of the state.
10. Establishment and enforcement of minimum sanitary standards for milk supplies.
11. Provision for services to aid industry in the study and control of health hazards due to occupation.
12. Prescription of qualifications for certain public health personnel.
13. Formulation of plans in co-operation with other appropriate agencies for the prompt mobilization of services to meet the health needs.

National, as distinct from state and local, health functions include at least the following :—

1. Study of national health problems and planning for their solution as may be necessary on a national scale.
2. Meeting the obligations assumed under the provisions of international treaties.
3. Control of communicable diseases in international and interstate commerce.
4. Administration of medical and health services on non-military national property and for certain classes of federal employees.
5. Discovery of the causes and means of control of disease through organized research.
6. Sanitary control of interstate traffic and common carriers.
7. Control of foods and drugs in interstate commerce.
8. Assistance to states, and through the states to local areas, in the extension or improvement of their health services. This assistance may be either technical or financial or both, as circumstances may require.
9. Central collection, tabulation, and publication of vital statistics of the various component political units (states or provinces, cities and rural areas).
10. Establishment of standards of control of manufacture and sale of biological products used in the treatment of disease.

Current Topics

Iron Exchanges of Adults on White and Brown Bread Diets

By E. M. WIDDOWSON

and

R. A. McCANCE

(Abstracted from the *Lancet*, Vol. I, 16th May, 1942, p. 588)

(THE authors of this paper are well known for their studies on the biochemistry of nutrition and were responsible for a most valuable monograph on 'The Chemical Composition of Foods'.)

In an experimental study of rationing carried out during the first six months of the war, they obtained some evidence that calcium was badly absorbed from a diet containing much brown bread. They then embarked on an investigation of the effects of flours of high extraction (containing a high proportion of the whole grain) on the mineral metabolism of man. A full account of these experiments and the data on calcium, magnesium, and phosphorus are published elsewhere. The results of the investigation of iron metabolism on white and brown bread diets may be summarized as follows:—

The iron balances of 4 men and 4 women were studied over a period of 9 to 12 months. The analytical periods were 7 days in length, and 3 or 4 consecutive weeks on each type of diet were employed, preceded by a preliminary period of 3 or 4 days. In all, there were ten 7-day periods on diets in which 40 to 50 per cent of the calories were derived from white flour, but which were normal in other respects and thirteen 7-day periods, otherwise similar, but in which brown flour of 92 per cent extraction replaced the white. It was found that all 8 subjects absorbed more iron from white bread than from brown in spite of the fact that the iron intakes were 50 per cent higher in the brown bread experiment. It is suggested that, in spite of the large amounts of iron in whole wheat flour, bread made from it may not be as good a source of iron as generally supposed.

The menstrual losses of 3 women were analysed for iron and were found to be characteristically different one from another, but very constant for any one woman from month to month.

Laboratory Investigations on Typhus

By G. M. FINDLAY

(Abstracted from the *Proceedings of the Royal Society of Medicine*, Vol. XXXV, December 1941, p. 157)

THIS paper by a leading British authority gives a clear and concise account of the laboratory methods employed in connection with louse-borne typhus fever.

(1) *Diagnosis*.—Proof that a disease is typhus can only be obtained by the isolation and passage through animals of the rickettsia. Two to five c.c.m. of the patient's blood is allowed to clot in the refrigerator; the clot is ground up in normal saline and injected intraperitoneally into a guinea-pig. In positive cases a febrile attack (40°C.) follows within 7 to 12 days. The virus is passed through a succession of guinea-pigs by intraperitoneal injection of 1.0 c.c.m. of equal parts of 10 per cent suspensions of the infected guinea-pig's spleen and brain. The animals show no naked-eye changes but sections of the brain have small collections of round cells. In murine typhus the guinea-pigs get orchitis as well as fever and the virus can be transferred through rats which react very slightly or not at all to exanthematic typhus. In Mexico and China, strains of rickettsia have shown features intermediate between those of murine and exanthematic typhus.

The commonly used test for typhus is the agglutination of proteus OX19: this should be positive within seven days, though delays in the response have been recorded, even up to 19 days. Titres up to 1-5,000 are frequent, they may even be as high as 1-100,000. With proteus OXK the reaction is negative or slight. In murine typhus the same reaction occurs, but usually in lower titres such as 1-200 to 1-2,000.

Positive Weil-Felix reactions also occur in undulant fever in titres of 1-80 to 1-240, but the progressive rise in titre does not occur. In typhus there may be a rising titre agglutination against typhoid organisms; in these anamnestic reactions the increase is almost entirely in the H agglutinins.

Agglutination of typhus rickettsia also occurs, but this test needs further investigation.

Typhus rickettsia injected intradermally into rabbits cause the formation of a nodule: if the rickettsia are mixed with serum from a recovered patient the nodules are not formed. The strength of the rickettsicidal bodies in a serum can be determined by using varying dilutions of the serum.

(2) *Special treatment*.—No effective chemotherapeutic treatment is known, convalescent serum has not been very useful, but the serum of horses which have been hyper-immunized with rickettsia from infected mouse lungs is being tried; there is a small stock of this serum in London.

(3) *Prophylactic immunization*.—Live murine rickettsia attenuated by passage through the brains of mice and treatment with egg yolk or by treatment with bile, also rickettsia from the faeces of infected lice have been used on a large scale, but there are no accurate figures to show their value and they are not free from risk in view of the possibility that murine rickettsia may be converted into exanthematic rickettsia by passage through lice.

Weigl's vaccine, prepared from the phenolized intestinal contents of lice infected per rectum with *R. prowazeki*, appears to be of considerable value, but this method involves a delicate technique and also the employment of a large staff of immune persons on whom the lice are fed.

Killed rickettsia obtained from the lungs of mice infected intratracheally or from cultures made in the yolk sacs of developing chicks are under trial, but the results, so far, are described as 'poor'.

Further research is needed to find a satisfactory method of immunizing against exanthematic typhus.

War Burns.—A Survey of the Treatment and Results in a Hundred Cases

By A. I. L. MAITLAND

(Abstracted from the *Journal of the Royal Naval Medical Service*, Vol. XXVIII, January 1942, p. 3)

THIS paper gives a detailed account of the treatment of 100 cases of burns in a Royal Naval Auxiliary Hospital. The cause in nearly all cases was bomb or shell flash, and the hands, face and ears were mainly affected. Most of the injuries had been sustained at least a day or two before admission to hospital. In three patients with symptoms of shock or toxemia, injections of eucortone (1 c.c.m. twice daily for two to four days) seemed to produce remarkable benefit. Apart from this, general treatment included a diet rich in first-class protein, abundant fluids by mouth (with glucose) and 100 mg. of ascorbic acid daily for all severe cases.

In 45 patients, including 21 with infected burns of third and fourth degree (Dupuytren), local treatment has consisted of cleansing, followed by painting of the burned area with 1 per cent crystal violet solution and powdering from an insufflator with 5 per cent sulphapyridine in boric acid. In late cases of infected third degree burns, this process, which is stated to produce a 'thin supple coagulum', has been repeated daily. It is claimed to have proved of great service in

reducing excessive granulation tissue and in sterilizing the discharge. The importance of early active movements in burns of the hands is strongly stressed. In a group of cases of infected third degree burns, received in hospital as long as three weeks or more after injury, a more complicated technique was employed in order to prepare the areas for skin grafting; this combined the uses of crystal violet and sulphapyridine, after careful cleansing under pentothal anaesthesia, with subsequent dressings with saline and with 1:4,000 acriflavine, and finally the application of wet normal saline packs over isinglass protective tissue.

Late tanning has been found satisfactory only in the absence of infection or when the latter has been effectively dealt with. Its chief value is in large clean superficial wounds of the trunk. Tannic acid is not recommended for burns of the hands or face, but the author refers to the difficulty of applying saline treatment *ab initio* in naval casualties. He suggests several alternative methods, which include repeated applications of triple dye or gentian violet for the first few days, followed by saline packs after admission to hospital, and the covering of the area with Thiersch grafts as soon as possible.

Complications of the burns in this series included 'blast chest' (14 cases) with, in five, the relatively common association of ruptured eardrums. As blast chest (compression effects in the lungs due to sudden violent changes in atmospheric pressure) is a contraindication to inhalation anaesthesia, intravenous pentothal has chiefly been used, where anaesthesia has been necessary during cleaning of the burns. The occurrence of defects of visual acuity has been noted after severe burns of the eyelids. Six cases of contracture of the hands were seen, and the author describes the treatment of a typical form of contracture by means of interdigital Thiersch grafts. Other trophic lesions of the hands, resulting from sepsis under a coagulum, included loss of nails, temporary hyperidrosis, Sudek's atrophy of the bones and gangrene of a finger tip (1 case). In summarizing his series, the author states that all cases of first, second and third degree burns which remained clean (63 per cent) gave good functional results; infected second degree burns (14 per cent) did likewise, but in a slightly longer time; infected third degree burns gave satisfactory results only when vigorous late treatment, other than tanning, was applied.

The Value of the Closed Plaster Method of Treating Air-Raid Casualties

By H. L. W. WOODROFFE

(Abstracted from the *Medical Press and Circular*, Vol. 206, 3rd December, 1941, p. 422)

The author reviews the history of the closed plaster method. It is said to have been first used by Ollier in the Franco-Prussian War and later by the French in the war of 1914-18 to a small extent. The method was then applied by Winnett Orr to civilian accidents. After the Spanish civil war, Trueta and others published a series of remarkable results obtained with it.

The essence of the method lies in three things, namely, removal as far as possible of all dead and foreign matter; absolutely free drainage; and complete rest of the injured part. If any of these three receives insufficient attention, failure is certain.

The edges of the skin are excised and all dead muscle is removed. It is unsafe to apply plaster unless this can be done completely; where it is impossible the Carrel-Dakin technique would be wisely adopted instead. Foreign bodies should be removed, but a search for them should not be damaging or prolonged. Haemostasis should be absolute. The clean wound should now be lightly packed, rather than plugged, with vaseline gauze, and the limb encased in a skin-tight plaster.

This method must not be used if there is doubt as to the viability of the limb or if there is established gas infection.

The first plaster will seldom require removal within a month, and at the end of this time a fracture, if it was present, should be sufficiently consolidated to avoid loss of position. Neither will there be much chance of activating latent infection. The wound should be dressed with full aseptic technique. There may be indications for an earlier change; the wound may not have been properly disinfected, the plaster may be too tight, or there may have been hæmorrhage. A small evening rise of temperature after injury is common, but signs of toxæmia demand immediate removal of the plaster.

If the patient is to be transported any great distance, the plaster should be split throughout the whole length, and the patient should be sent only where surgical facilities are available.

The advantages of the method include almost complete freedom from pain and the avoidance of repeated dressings; moreover, the enforced rest promotes healing. The persistent smell, however, is a disadvantage and the patient may also develop a transient dermatitis round the wound. Occasionally the primary reduction is not maintained and a further reduction is necessary.

The author considers that the advantages of the method outweigh the disadvantages, and he details four illustrative case histories.

Sulphadiazine

By E. E. NELSON, M.D.

(From the *International Medical Digest*, Vol. XL, May 1942, p. 308)

In the issue of the Journal of the American Medical Association for 28th February, 1942, the Council on Pharmacy and Chemistry announced its acceptance of sulphadiazine for inclusion in New and Non-Official Remedies. Previously the Food and Drug Administration had released sulphadiazine for distribution and sale in interstate commerce. Thus a new member of the sulphonamide group has been made generally available to the medical profession. The above-mentioned actions of these two agencies are both reasonable indications that a fairly considerable body of information concerning the new drug exists, that it gives some promise of being a real addition to therapeutic agents, and that possible hazards in its use have been given consideration. The purpose of the present article is to review some of the published reports, which undoubtedly contain much of the evidence on which the Council on Pharmacy and Chemistry and the Food and Drug Administration have based their respective actions.

Sulphadiazine, chemically speaking, is 2-sulphanil-amido-pyrimidine, an analogue of sulphapyridine. One of the hydrogens of the sulphonamide group of sulphanilamide has been replaced by a pyridine in sulphapyridine, and by pyrimidine in sulphadiazine. The substance is a white crystalline powder, only slightly soluble in water (0.0123 gm. in 100 c.cm. at 37°C.). The sodium salt, however, is readily soluble. The absorption, distribution, and excretion of sulphadiazine have been extensively studied in both laboratory animals and man. Although there is a rather considerable amount of individual variation in both rate and completeness of absorption, in general it may be said that the drug is taken up from the gastrointestinal tract to a satisfactory degree. Most observers believe absorption to be somewhat slower than that of sulphanilamide or sulphathiazole. Therapeutically effective blood concentrations are reached in 2 to 4 hours and maximum blood concentrations from single oral doses in 3 to 6 hours. Excretion is chiefly by way of the kidney, but is slower than that of the other sulphonamides. Reinhold *et al.*, for example, found that on the average less than 50 per cent of a single dose is so excreted in 24 hours, whereas 60 to 90 per cent of an equivalent dose of sulphathiazole appears in the urine in this period. As is the case with the other sulphonamides, sulphadiazine

is in part acetylated in the body, and occurs in blood, urine, and other fluids both in the free and conjugated forms. The ratio of free to total sulphadiazine has been examined many times. Working with monkeys, Feinstein and his collaborators found that less than 10 per cent of the drug in the blood stream after single doses was in the conjugated form. A similar situation holds in the human species, although the percentage of bound drug may run higher. However, there is so little difference between free and total values in the blood that the latter determination is said to suffice for clinical purposes. Feinstein noted the relatively high solubility of acetyl sulphadiazine in urine as compared with other acetyl sulphonamides. Apparently it is very easily excreted in the urine, and perhaps for this reason does not tend to increase in amount in the blood stream on continuous administration.

Because of the satisfactory absorption, slow excretion and small degree of acetylation, it is relatively easier to obtain and maintain high blood levels after sulphadiazine than it is after the other sulphonamides. Spink calls attention to the necessity for recognizing this fact if one follows the schedules of dosage which have become more or less standardized for sulphapyridine and sulphathiazole.

The distribution of sulphadiazine in tissues and body fluids is somewhat irregular. Diffusion into the cerebrospinal fluid is slow. After single oral doses of 4 gm. given to patients without evidence of acute inflammation of the meninges, Sadusk and Tredway found the total sulphadiazine in the cerebrospinal fluid at 4 hours to be from 3 to 15 per cent of that in blood. With continued treatment, however, the percentage rose so that the percentage at 24 hours was from 42 to 53 per cent of that of blood. The same workers noted that after an intravenous administration of sodium sulphadiazine, higher cerebrospinal fluid concentrations were attained at the end of 4 hours. Peterson *et al.* and Long obtained somewhat higher values than those of Sadusk and Tredway. The Council report places the ratio of cerebrospinal fluid to blood content as one-half to four-fifths. It is evident that penetration into the cerebrospinal fluid is satisfactory. Further, the conjugated fraction remains low. Sulphadiazine also occurs in pleural, abdominal, and synovial fluids.

One of the greatest advantages claimed for sulphadiazine is its relatively low toxicity. This was claimed for animals, in both acute and chronic toxicity studies, in the original report of Feinstein *et al.*, and has been generally confirmed clinically. For example, in the series of 446 patients with various infections treated by Finland and associates, nausea and vomiting occurred in less than 10 per cent, hematuria in less than 1 per cent, leukopenia in 2 per cent. Morbilliform eruptions were seen in 9 cases, occurring about the eighth day. In a series of 137 cases of pneumococcal pneumonia treated with sulphadiazine, Dowling and associates report even a smaller percentage showing nausea and vomiting, and all other reactions were mild and transitory. The lack of evidence of renal injury by the drug has frequently been a matter for comment. A few cases of drug rash and drug fever have been reported. Flippin and associates in a comparison of sulphathiazole and sulphadiazine in pneumonia reach the admittedly tentative conclusion that the latter substance is somewhat more likely to induce a drug psychosis. Apparently the experience of others has not confirmed this first impression. Serious blood changes do not seem to be frequent, and, according to the Council report, only one case of agranulocytosis has been noted.

The first experimental work on animals indicated that sulphadiazine had therapeutic activity against experimental pneumococcal, streptococcal, staphylococcal, and Friedländer's bacillus B infections in mice. Subsequent clinical investigations have established the laboratory indications. According to Spink, sulphadiazine is as effective as sulphapyridine and sulphathiazole in the treatment of pneumococcal pneumonia.

Flippin *et al.*, comparing the results in the treatment of 100 adults with pneumococcal pneumonia with sulphadiazine with a similar series treated with sulphathiazole, had a mortality of about 6 per cent in the sulphadiazine series as compared with 11.5 per cent in the sulphathiazole series. Deaths occurring in patients hospitalized for less than 24 hours have been excluded from both series. These workers note that sulphadiazine tends to lower the temperature somewhat more rapidly than sulphathiazole. Long, in the preliminary report of the Council, expressed his belief that sulphadiazine was slightly less effective than sulphapyridine or sulphathiazole in the treatment of pneumococcal pneumonia. Finland *et al.* and Dowling *et al.* find the three drugs to be about equivalent in therapeutic results, though the last-mentioned workers believe that sulphadiazine is to be preferred because of the lack of toxic side-effects.

Experience in the treatment of other types of infection is as yet somewhat limited. Sulphadiazine is said to be highly effective in both streptococcal and staphylococcal pneumonias, and as effective as sulphamylamide in the treatment of hemolytic streptococcal infections. Finland and associates, whose published results are apparently the most varied of any yet available, include 'meningococcal infections; acute infections of the upper respiratory tract including sinusitis; erysipelas; acute infections of the urinary tract, particularly those associated with *Escherichia coli* bacilluria, and acute gonorrhoeal arthritis' among those diseases in which sulphadiazine appears to be highly effective. Dingle, Thomas and Morton treated 13 patients with meningococcal meningitis and one with meningococcal bacteremia with one death, occurring 10 hours after admission. In gonorrhoeal urethritis in the male, LaTowsky and his associates have found sulphadiazine to be extremely effective. Of 55 cases, 51 were considered cured after an average of 8 days of treatment. The criteria of cure were two or more negative smears and two negative cultures of prostatic fluid. The total amounts of drug required varied from 4 to 58 gm. Toxicity symptoms consisted only in an occasional headache. Recently Pickrell has reported the successful use of a sulphadiazine spray in the treatment of second and third degree burns. A 3 per cent solution of sulphadiazine in 8 per cent triethanolamine is sprayed directly on the burned areas. It reduces the pain to a considerable degree. The treatment is repeated at definite intervals through the fourth day. A thin translucent eschar is formed through which the process of healing can be observed. This protective covering is elastic and pliable. The material is said to be without harm to mucous membranes or granulation tissue, and can be safely used about the eyes. The results are said to be better than those from any other method of handling second and third degree burns. The interested reader should refer to the original paper for details of the procedure.

The doses of sulphadiazine which have been used up to now are about the same as those generally used for sulphapyridine and sulphathiazole. In the Council report it is suggested that in the treatment of pneumococcal pneumonia 0.10 gm. per kg. be given as the initial dose, to be followed at 4-hour intervals by doses of 1 gm., to be continued until the temperature has been normal for 72 hours. In children an initial dose of 0.10 to 0.15 gm. per kg. is suggested, to be followed at 6-hour intervals by one-quarter of this amount, until the temperature has been normal for 48 hours. For less severe infections smaller amounts may be adequate. A blood level of 15 mg. per 100 c.c. should be reached and maintained in severe streptococcal and meningococcal infections.

In summary, it seems that this new agent is at least as effective as the older sulphonamides in many conditions, and in addition it has in its favour less tendency than the better known members to cause unpleasant or dangerous side reactions. Further experience will serve more clearly to define its position in modern therapeutics.

The Treatment of Shock in Air-Raid Casualties

By F. RONALD EDWARDS, M.D., Ch.M., F.R.C.S.
(From the *Medical Press and Circular*, Vol. 208,
1st July, 1942, p. 3)

MODERN warfare, particularly aerial bombardment, tends to induce, by continuous apprehension, loss of sleep, and cold, a predisposing state for the development of shock should a wound be incurred. Most casualties, when admitted to a first-aid post or hospital, are suffering from some degree of shock, although many are mild. These mild cases with slight wounds only, are usually shivery, somewhat nauseated, and rather pale, a state described by the patient as the 'reaction'. Reassurance, dressing of the wound, a cup of hot sweet tea, and a sit down will usually put them to rights and allow their return home. Some 30 per cent of all living casualties will, however, call for more active treatment.

In the first-aid post much can be done towards the alleviation of shock by relieving pain. Morphine grain $\frac{1}{4}$, or even in some cases grain $\frac{1}{2}$, should be given to this end. Splinting of fractured limbs, as rapidly as possible, is necessary. Attempts to perform reduction of the fracture or splinting in the ideal position, if this causes pain to the patient, will do more harm than good. Fixation of the traumatized member is the main object, so that pain will not be produced during transference to hospital. Bleeding must be stopped, and this is done most satisfactorily by pressure over the bleeding point with a large pad of wool and a very firm bandage. Only if this fails to control the hemorrhage is it wise to use a tourniquet. A tourniquet produces much pain, and needs a fair amount of strength to put it on efficiently, a procedure which necessitates considerable movement of the limb and suffering to the patient. The administration of fluids is an important factor in early resuscitation, and this should be given as strong hot tea, well sweetened, but it is important to exclude an abdominal injury before this is given. Actual transfusions are difficult to undertake in a first-aid post, and should be reserved until the patient reaches hospital. Warmth is essential, and plenty of blankets and hot water bottles should be ready at hand as soon as the raid starts. The post itself must be kept really warm. Open chest wounds must be immediately closed with a few sutures, or by a firm pad of wool, or by vaseline gauze well fixed by strapping placed over it in layers, for in such a condition the swinging of the mediastinum, paradoxical respiration, and inefficient air entry induce an anoxic state which makes the degree of shock infinitely more severe. Oxygen is of great value in these cases, and should be continued if necessary during the ambulance journey to hospital.

Cases suffering from severe shock have the first call on the ambulances. 'Severe shock' must be distinguished from 'moribund'. It is bad policy to prejudice the chances of cases that have a reasonable chance of recovery by sending by the first ambulances cases that are so severely injured that they have practically no chance of surviving. The decision in such cases depends upon the clinical experience of the Medical Officer, and he should assess fully the probable prognosis in each case; this may be difficult, but, for example, it is probable that a case of shock, due to severe limb injuries and loss of blood, has more chance of ultimately surviving following effective resuscitation therapy than a case of shock due to an extensively lacerated abdomen.

On admission to the hospital rapid examination, administration of A.T.S. and ligation or pressure-dressing of bleeding points is undertaken, and all cases suffering from shock are sent to the resuscitation ward. There is a small group of cases, who although suffering from extensive injuries, appear not to be shocked on admission to the hospital. Such cases should also be admitted to the resuscitation ward, for they will certainly become shocked, both suddenly and severely, within the next one to two hours.

The utilization of special shock teams in the resuscitation wards has greatly improved the treatment of these patients because more time and attention can be given to the therapeutics of this syndrome. The necessary attribute for membership of a shock team is facility with an intravenous needle and cannula and an experience with the vagaries of the transfusion apparatus. Thorough training is necessary. A man who has not the ability to take less than half an hour in setting up a transfusion apparatus has no place in the shock team. With the necessary apparatus ready sterilized he should so train himself as to be able to set up a transfusion by cannula in ten minutes.

Warmth and the elimination of external stimuli are important. The ward itself must be warm, and it is advisable to have spare paraffin stoves available if the usual method of heating becomes affected by heavy bombing. All lights must be shaded, and again accessory portable lighting must be at hand. (Remember to have all emergency equipment tested once a week.) It is a good plan to plug the ears of each patient with cotton-wool on entry, as the cries of other injured people are very distressing.

The immediate resuscitation of the patient is the primary object, and removal of the clothes and dirt are a secondary factor. The casualty is warmed up by hot water bottles and a heat cradle. Too much heat makes the patient uncomfortable, and four lamps are usually quite enough. Again, drinks of sweetened tea are given freely, provided there is no abdominal injury. In some cases this may induce vomiting, and it is well in such people to restrict the fluids by mouth. The administration of morphine may have to be repeated, particularly if the patient is restless, and it is not contraindicated in any condition except head injuries. Morphine may be given to patients with chest injuries provided that the respiratory rate does not become too slow. In most cases raising of the foot of the bed will help in the resuscitation, but in chest injuries this position may not be tolerated by the patient, and it may be necessary, in order that he can breathe at all comfortably, to prop him up on a back rest.

The pulse rate and blood pressure are charted every half-hour. A systolic blood pressure below 80 millimetres of mercury is an indication for intravenous administration of blood or plasma, but any case of extensive injury should receive transfusions, even though the blood pressure may be normal. These latter are the cases described before in which the natural vaso-constrictor substances in the body are playing a gallant but losing fight against a steadily falling blood volume. It is better to prepare for the circulatory collapse beforehand, in order to lessen its severity, and its onset may even be prevented, if the intravenous therapy has been adequate enough. Casualties suffering from burns, too, may have a normal or even raised blood pressure, but even those cases with moderate involvement of tissue should have intravenous fluid administration. In severe degrees of shock the first two pints of blood should be given as fast as possible, and then the transfusion continued at the rate of one pint every half or three-quarters of an hour. Excellent results have been obtained in apparently moribund patients by the insertion of two or three cannulae and the forced administration of four to five pints of blood or plasma in half to three-quarters of an hour. Only when the systolic blood pressure has reached the level of 110 millimetres of mercury, the pulse rate is falling, and the pulse volume is increasing, is the patient ideally suitable for a major operative procedure. It must be remembered, too, that in old people the normal blood pressure may be considerably in excess of this figure owing to arteriosclerotic changes, and it is a fine point in treatment of such casualties to be able to assess by clinical examination their probable pre-traumatic blood pressure.

A very severe degree of shock will develop if an insufficiently resuscitated patient is anaesthetized and operated upon, unless special precautions are taken. The only indications for doing this are, firstly, to

ligate bleeding vessels that cannot be controlled without recourse to operation, and secondly, abdominal injuries. An abdominal injury should be operated upon within six hours of injury, and it is inadvisable to wait after this time before exploration is undertaken. Where urgent operation is necessary, the transfusion must be maintained throughout the operation and after. Any loss of blood during the operation must be made up by increasing the speed of the transfusion to the maximum.

Blood is in all cases, except burns, a better resuscitating agent than plasma. But the supply of blood is always limited, owing to the limit of effective storage being fourteen days, hæmolytic of the red cells beginning to take place after this time. Plasma will keep indefinitely, and consequently large stocks can be accumulated for emergency purposes. Therefore blood should be kept for those cases in which hæmorrhage is the main factor in the collapsed state, as assessed by the blood-stained condition of the clothes and the anatomy of the wound. Plasma is suitable for all other cases, and in particular burns, where no erythrocyte loss has occurred. If casualties are admitted in any number, grouping of the recipient is impossible, and group 4 blood should be administered. Plasma is nowadays pooled, and can be safely administered to patients of any group. Reactions to transfusion either of blood or plasma are very rarely seen in shocked casualties, and if there is evidence of a rigor developing, or severe pain in the back, then there is something essentially wrong with the transfusion fluid, and it should be immediately discarded.

POINTS IN TECHNIQUE

The standard transfusing outfit in use throughout the country is the one supplied by the Ministry of Health. It has proved eminently satisfactory in use. Administration by means of a needle fixed into the antecubital vein does, however, often give rise to trouble during the transfusion of casualties. Such patients tend to be very restless, and even though the arm may be splinted, spontaneous movements may force the needle out of the vein with formation of a hæmatoma, and the almost certain impossibility of re-entry in that area. Many cases of shock, too, have such collapsed veins that it is difficult to make a clean perforation of the vein wall through the skin, and it is only too common to see the posterior wall transfixed also. My own personal preference is to always use a cannula in these traumatic cases. A large number of sterilized cannulae made of either silver or glass should be kept ready and substituted for the needle of the transfusion set after it has been taken out of its sterile packing. The internal saphenous vein in the front of the internal malleolus is exposed and the cannula tied in. The tubing leading from this is fixed to the dorsum of the foot by four pieces of strapping and led off between the great toe and the second toe. By this means secure fixation is established. The transfusion apparatus is then well out of the way and is in the most comfortable position for the patient. No splinting of the leg is usually necessary, but if the patient is extremely restless, the foot can be bandaged to the end of the bed. This firm fixation of the cannula also lessens the chances of the transfusion being interrupted during transit from the resuscitation ward to the theatre or from the theatre to the general ward, for in most cases the transfusion will have to be continued during the operation and for some hours afterwards, either as blood or plasma, or 5 per cent glucose saline. Owing to the collapsed veins again there may be some difficulty in getting the transfusion to flow at first. It is best started by squeezing down the tube and forcing open the veins with the transfusion fluid and is further aided by keeping the foot of the bed raised. The bottle should be at least 30 inches above the vein. Any tendency for the rate of flow to fall below that which is required is remedied by squeezing down the tubing, and this procedure will free the end of the

cannula or needle of the gelatinous deposit which collects there.

OXYGEN THERAPY

Many cases are helped by oxygen administration by the B.L.B. mask or by the Tudor Edwards spectacle frames. The use of a funnel in front of the face is a waste of time. If an intra-nasal catheter is used it should be well lubricated with percaïne jelly, as otherwise its presence in the nares may be highly irritating to the patient. The primary indication for oxygen therapy is a thoracic injury, but any case of shock from other causes, in which cyanosis is noted, will be considerably helped. Oxygen should flow at six to eight litres per minute, and if the B.L.B. mask is used all the ports are closed. If oxygen has been necessary in the resuscitation ward this must be continued during transit to and from the theatre, and a portable oxygen apparatus is a very necessary part of the equipment.

Drugs

Vaso-constrictor drugs have been disappointing in their effect in established shock, and adrenalin itself is definitely contra-indicated. Cardiac stimulants are of doubtful value as the heart itself is unaffected in the shock syndrome except secondarily to the reduced blood volume and anoxic blood in the coronary circulation. Eucortone (1 c.c. intramuscularly) has been advised, but further experience has cast doubt on its value in shock, although its adjuvant use in burns has more favourable acceptance. Morphine is the drug of real value, and more lives have been saved by this agent than by all the others.

ANÆSTHESIA

Where an operation is likely to be prolonged, an anæsthetic with a very high oxygen content must be used, and cyclopropane and oxygen is the one of choice. For a short anæsthetic, open ether or ether and oxygen is probably the best, as for the first half hour ether has a stimulant action, after which time, however, there is a great tendency to increase the depth of the shock. Most operations should be completed in this time, for there is no place for the dilatory surgeon in the treatment of war casualties. Experience has suggested that gas and oxygen is an unsuitable anæsthetic for patients recovering from shock, as the necessary depth of anæsthesia necessitates some degree of anoxia, a factor against which we are continually struggling in the treatment of shock. If casualties are few and time is available, surgery conducted under local anæsthesia as far as possible, has much to recommend it, as most certainly the degree of operative shock superimposed on the traumatic shock is thereby diminished.

The main essential in the early treatment of war casualties is that the surgeon be presented with a patient, who has been brought into such a condition that he will safely stand the necessary operative procedure. Surgery in the greater proportion of casualties is not a matter of instantaneous urgency, and the time spent in the careful and controlled resuscitation of these patients will be well repaid by a recovery in a very high percentage of serious injuries.

The Treatment of Scabies

By K. MELLANBY

C. G. JOHNSON

and

W. C. BARTLEY

(Abstracted from the *British Medical Journal*, Vol. II, 4th July, 1942, p. 1)

THERE is considerable uncertainty regarding the best methods of treating scabies, and a full summary of recent literature on the treatment of this condition has recently been given, by Gordon and Seaton, who have studied the effect of different treatments on *Notoedres* infestations in animals.

Scabies is, however, caused by an invasion of the human cuticle by the parasite *Sarcoptes scabiei de G. var hominis*, and a final estimation of the value of various treatments must be assessed by their ability to kill the parasite under clinical conditions. The present authors have developed methods by which they believe that over 90 per cent of the adult female parasites can be detected, and in their experiments they have assessed cures by examination of the parasites removed from human cases. Most of the adult female *Sarcoptes* infesting each case were removed and examined twenty-four hours after treatment and the proportion killed was noted. Those medicaments which were efficient gave equally good results when applied to the skin without preparatory bathing or scrubbing.

A single thorough application of 10 per cent sulphur ointment, of Marcussen's ointment, of benzyl benzoate of any strength greater than 10 per cent made up either in a spirit solution or in a watery emulsion, or of dimethyl diphenylene disulphide, killed over 98 per cent of the parasites. The following substances were found less effective:—Pyrethrum, rotenone emulsion, derris root lotion, beta naphthal and lethane. Methods which produced a coating of sulphur particles on the body (dusting with precipitated sulphur, painting with thiosulphate followed by hydrochloric acid, sulphur foam tablets) were found very inefficient. Sulphur taken internally had no effect on *Sarcoptes*.

To paint on a benzyl benzoate emulsion requires some skill and unless trained personnel is available it is sometimes advisable to use a sulphur ointment which, even if applied inefficiently, will work itself all over the body. Not more than two applications of an efficient medicament are required, though it should be noted that in many patients symptoms such as itching may take many days to disappear, but they do disappear eventually without any further treatment.

Anæsthesia in Aged Patients

By H. B. ALCOCK

(Abstracted from the *Medical Press and Circular*, Vol. 208, 15th July, 1942, p. 44)

THE author refers to the following general considerations, which are of special importance in elderly patients:—

(1) The aged are usually placid and co-operative subjects.

(2) They require less anæsthetic. Elimination is slow, because of the lowered metabolic rate.

(3) Abundant oxygen is necessary, particularly if shock is present.

(4) Powerfully narcotic and depressant drugs as prophylaxis against chest complications should be avoided, particularly in those with pre-existing chest trouble.

(5) The avoidance of toxic drugs in such conditions as diabetes, uræmia, abdominal emergencies, etc., is important in all patients, but particularly so in the aged.

Pre-medication. The following points are stressed:—
(1) The importance of pre-operative glucose and sedation.

(2) The pernicious effect of excessive starvation and purgation.

(3) The administration of morphia and atropine 1½ hours pre-operatively.

(4) The avoidance of depressive basal hypnotics.

(5) The usefulness of pentothal for induction.

Choice of anæsthetic.—Nitrous-oxide oxygen is recommended by the author as it is non-toxic. For abdominal surgery, however, it must be supplemented and for this the following are available:—

(1) Chloroform and di-ethyl-ether are condemned—the first for its high toxicity, the second for toxicity and irritant qualities.

(2) Cyclopropane, di-vinyl-ether and trichlorethylene are all valuable, though with the last, relaxation may not be perfect.

(3) 'High' spinal anæsthesia is risky owing to the strain imposed on the vascular system. 'Low' spinal anæsthesia, for example, for hæmorrhoidectomy, is permissible.

(4) Regional analgesia is suggested as the best supplement to nitrous-oxide oxygen. Techniques suitable for most conditions are easily acquired and the method is safe even in unpractised hands if due precautions are taken.

Megaloblastic Anæmia of Pregnancy and the Puerperium

By L. S. P. DAVIDSON

L. J. DAVIS

and

J. INNES

(Abstracted from the *British Medical Journal*, Vol. II, 11th July, 1942, p. 31)

ANÆMIA occurring in pregnancy and the puerperium in temperate climates, apart from the apparent anæmia caused by physiological dilution of the corpuscles resulting from the increased plasma volume of pregnancy, is usually of the hypochromic iron deficiency type. Very rarely it may be of the classical Addisonian pernicious variety, but more often while resembling this type it differs from it in certain features and is often named 'pernicious anæmia of pregnancy'.

In the present paper, Professor Davidson and his colleagues describe 16 cases of this latter variety of anæmia seen at the Department of Medicine, Edinburgh University. The anæmia was severe in all cases. Analysis of the peripheral blood findings indicated in many of the cases a dual deficiency of liver and iron, for while macrocytosis and a high colour index were frequent, these features were not so pronounced or so constant as in classical Addisonian pernicious anæmia. In some of the cases the colour indices were below unity. Free hydrochloric acid was also present in the gastric juice of many of the cases. A constant finding, however, was a megaloblastic picture in films made from the sternal marrow obtained by sternal puncture. Accordingly the name 'megaloblastic anæmia of pregnancy and the puerperium' has been proposed for this type.

Many of the cases were temporarily refractory to treatment with liver extract, iron and other hæmatics, but persistence with such treatment and maintenance of life with blood transfusions when necessary, eventually resulted in complete recovery in all the cases with the exception of two in which death resulted from incidental causes.

A Nutritional Investigation of the Antibacterial Action of Acriflavine

By H. McILWAIN

(Abstracted from the *Biochemical Journal*, Vol. XXXV, December 1941, p. 1311)

STUDIES of the mode of action of chemotherapeutic agents, based on the hypothesis that they interfere with metabolites essential to pathogenic organisms, have recently been successful in interpreting the antibacterial action of sulphanilamide and mercuric salts.

It is shown that inhibitory agents cause fresh nutritional needs in the affected organisms, and that when these are satisfied growth can take place in the presence of an otherwise inhibitory concentration of therapeutic agent ('reversal' of the inhibitor). There is now among British workers a general realization that therapeutic agents may act by affecting metabolic processes, and the present method of investigating their action is now available. Thus Ehrlich suggested that the normal function of the 'receptors' was nutritive, though he later abandoned,

or failed to emphasize, this view. Metabolic ideas have more recently been applied to acridine compounds. Analogous conceptions of enzyme interference have also successfully explained the pharmacological actions of eserine as due to blocking of choline esterase.

The acriflavine drugs were developed as trypanocides, but their main current use is as antiseptics. *Bact. coli* and *Streptococcus hæmolyticus* were the organisms mainly used in the work described in detail in the present paper. Acriflavine (here used as a general term) is a mixture of 2,7 diamino-acridine, proflavine, and its 9-metho-chloride which is sometimes, as in this paper, referred to as euflavine. Slight differences in the actions of the two compounds have been described. The present work was mainly carried out with euflavine; the conclusions were found applicable to proflavine.

Bact. coli and *Streptococcus hæmolyticus* were grown in the simplest available media adequate for optimal growth. The inhibitory effect of acriflavine components was found to be annulled by extracts of yeast, liver, etc., and chemical fractionation of these extracts showed that their activity was due to two types of material: (1) nucleotides, which the author considers to act by forming complexes with acriflavine and (2) an amino acid fraction, which the author regards as the substrate or product of enzymes to the inactivation of which these concentrations of acriflavine owe their activity. Inhibition by higher concentrations of acriflavine cannot be reversed by the amino acid fraction alone, but can be reversed by this fraction together with hydrogen carriers. The latter do not function alone either, and the author considers that they replace hydrogen transporting systems which have been inactivated by acriflavine. This work supports the view that chemotherapeutic agents inhibit micro-organisms by depriving them of the use of enzymes or metabolites by various types of interference.

Treatment of Burns

By H. C. HULL

(Abstracted from the *Archives of Surgery*, August 1942)

BASED on an analysis of 188 cases of burns encountered from 1930 to 1939, in contrast to a comparable series of 92 cases occurring from March 1939 to November 1941, the author reviews the present standards of treatment. Three surgical principles are emphasized in the treatment of burns: (1) the primary treatment of shock before considering treatment of the burned area; (2) the recognition of a burn as an open contaminated wound, which should be properly cleaned before treatment; (3) the choosing of a sterile and non-irritating agent for the treatment of the burned area.

Patients with severe burns when first seen should be given morphine, should be wrapped with some covering (no greasy preparation should be applied to the burn) and should be sent as rapidly as possible to a hospital where proper shock therapy can be given.

Plasma therapy in the treatment of shock due to burns has, as in this series, definitely lowered the mortality rate. Infants and children are particularly liable to shock and should be treated for it whether or not they exhibit clinical signs. Though the reported mortality rate of 13 per cent is in no way remarkable, deaths from shock have dropped to 3 among the last 92 patients treated compared with 27 among the previous 188.

Cleaning of a burn should not be undertaken until the patient is responding well to shock therapy. Cleansing should be done under aseptic conditions as quickly, gently and thoroughly as possible.

Eschar-producing agents are preferred at this clinic for the treatment of burns involving multiple areas. They should not, however, be used on the fingers, the hands, the toes, the feet or the face. These agents do not replace destroyed tissue, and after their use the

patient must be watched daily for all complications that can develop in the stage between the accident and the cure. Pneumonia complicating burns in infants and children has proved rapidly fatal in spite of modern therapy.

Patients with third degree burns can be spared many weeks in the hospital by skin grafting performed as soon as the condition of the patient permits.

It is a prediction that hospitalization for patients with burns will be prolonged in the future, because some of the severely burned patients who died from shock in the past will now be saved owing to improved methods in shock control.

Sublingual Testosterone Therapy of Male Eunuchoids

By H. LISSER

R. F. ESCAMILLA

and

L. E. CURTIS

(Abstracted from the *Journal of Clinical Endocrinology*, June 1942)

THE authors had reported the sublingual administration of testosterone propionate, methyl testosterone and free testosterone, each dissolved in propylene glycol so that 0.2 c.c. contained 5 mg., in daily doses ranging from 10 to 25 mg. Five typical eunuchoids whose condition previously had been improved and who had been successfully maintained by parenteral, implantation and/or oral administration of testosterone compounds, continued their improved states on sublingual testosterone. In only 1 of the 5 cases was the sublingual mode of therapy more economical in milligrams required than the peroral route. All the patients preferred swallowing tablets to dropping a solution under the tongue. Four hypogonadal patients who had not previously received any testosterone therapy derived striking benefits subjectively and objectively from the sublingual administration of testosterone compounds. Larger oral doses of methyl testosterone would have been required to accomplish equivalent results. Sublingually, free testosterone was more effective than either methyl testosterone or testosterone propionate.

Observations on the Chemotherapy of Trachoma

By A. R. McKELVIE

R. KIRK

and

H. J. HOLDER

(From the *American Journal of Ophthalmology*, Vol. XXIV, September 1941, p. 1035)

INTRODUCTION

SINCE Lian in the Dutch East Indies, Loe in America, and Kirk, McKelvie and Hussein in the Sudan reported independently that sulphonamides have a remarkable effect in the treatment of trachoma, a considerable literature has accumulated on the subject. A number of criticisms have been raised, but the original observations have been amply confirmed. Although sulphonamides taken by the mouth may not cure every case of trachoma, they have already taken a useful place in the treatment of this disease, particularly in cases with corneal complications, such as pannus and keratitis.

The scope of our earlier communication was restricted merely to recording what appeared to be a remarkable reaction to chemotherapy in a supposed virus disease. No attempt was made to explain this, or to compare the results in detail with those obtained by other methods of treatment.

During the past two years attempts have been made to investigate more fully the action of sulphonamides in trachoma. The inquiry has proceeded along two main lines. The first, largely clinical, is to assess the effect of sulphonamide therapy in different varieties of the disease, in order to separate the types that are likely to derive most benefit from the drug from those in which the benefit is slight or doubtful. The second, of more theoretical interest, is to determine how these compounds act, whether they influence directly the causal agent of trachoma or merely eliminate the effects of superimposed bacterial infection.

Since the so-called virus of trachoma cannot be grown in artificial culture media or maintained in any of the laboratory animals at our disposal, the work has necessarily been restricted to clinical and laboratory observations on trachoma patients coming to the Ophthalmic Department of Khartoum River Hospital. Many of the observations are incomplete, since clinical experiment must always be subservient to the primary functions of the hospital; namely, treatment and the prevention of complications, of which blindness is the most serious and important.

The general trend of these observations has been to amplify rather than alter any of the conclusions reached in our earlier paper, without producing any definite evidence as to the manner in which sulphonamides act in trachoma. For this reason it was our intention to defer publication until further data had been accumulated, but since the outbreak of hostilities in East Africa it is unlikely that it will be possible to continue this work. The data already accumulated, however, are not without interest. At the present stage it is possible to indicate those types of the disease as seen in this country in which sulphonamide therapy is beneficial, and those in which it has little or no effect. In addition, a number of observations have been recorded which may have some bearing on the manner in which cure is effected.

DOSAGE AND TOXICITY

Three compounds were used, sulphanilamide (Prontosil album), prosectasine (M.&B. 125), and sulphapyridine (M.&B. 693). No difference in therapeutic effect could be noted among the three drugs so in the observations which follow they are all referred to as sulphonamide, and no differentiation is made between cases treated by one or other of the compounds. No hard-and-fast scheme of dosage was used, but as a result of previous experience the following tentative system was adopted as a basis:—

(a) *Sulphanilamide* (Prontosil album). For adults, one tablet (0.5 gm.) thrice daily; for children 10-15 years, half a tablet (0.25 gm.) thrice daily; and for children 5-10 years, half a tablet (0.25 gm.) twice daily. Initial course up to a maximum of 21 days, followed by a rest period, and then, if necessary, further treatment among similar lines.

(b) *Prosectasine and sulphapyridine*. For adults, four tablets (2.0 gm.) a day, at the rate of one tablet (0.5 gm.) at four-hour intervals, for a period of 15-21 days; for children 10-15 years, one and a half tablets (0.75 gm.) daily in half-tablet (0.25 gm.) doses at four-hour intervals; and for children 5-10 years, one tablet (0.5 gm.) daily, given in two half-tablet (0.25 gm.) doses, separated by four-hour intervals.

It was found that the rapidity with which individual patients react to treatment varies within wide limits. For this reason the aforementioned schemes of dosage were not followed rigidly in all cases, but were regarded as tentative systems which could be modified according to the clinical progress in individual cases. Better results are undoubtedly obtained in this way than by the adoption of a standard routine treatment for all cases.

Toxic symptoms have been almost negligible; nausea occurred in a few instances but disappeared when the treatment was stopped; toxic skin manifestations were seen once in a European patient, but not in the Sudanese. Routine blood examinations were not carried out.

SULPHONAMIDE THERAPY IN COMPLICATED TRACHOMA

By complicated trachoma we mean trachoma complicated by some other affection of the conjunctiva. In the present observations, pathological rarities are excluded, and the only superimposed conditions which need be considered are secondary bacterial infection and the so-called spring catarrh or vernal conjunctivitis. According to Wilson, trachoma in Egypt is essentially a chronic disease which generally commences and often progresses so insidiously that the patient is unaware of his infection. This is true in the Sudan also. In the vast majority of our cases, the patients present themselves at hospital only when the trachoma has become complicated by secondary infection, and when the latter clears up regard themselves as cured, and cease to attend for further treatment.

Secondary bacterial infection.—In cases of trachoma complicated by secondary infection, it is rarely necessary in the Sudan to use cultural methods to identify the causal bacteria, since this can generally be done more rapidly by the examination of stained smears from the conjunctival exudate. The type and frequency of the bacteria concerned in a series of 200 such cases treated by sulphonamides were shown to be: gonococcus, 18.5 per cent; Koch-Weeks, 65.5 per cent; pneumococcus, 2 per cent; Morax-Axenfeld, 14 per cent.

It may be pointed out here that the discovery of a particular organism in the conjunctiva does not necessarily justify the conclusion that this is the cause of any pathologic condition which may be present. A number of the cases in the present group could be described clinically as 'flare-up trachoma' rather than trachoma complicated by purulent ophthalmia. Since organisms were readily found in these cases, and the reaction to sulphonamides was similar to that of the purulent ophthalmias, we have not differentiated between the two conditions.

Sulphonamide therapy has a rapid curative effect in cases of trachoma complicated by secondary infection. This conclusion is derived from the observation of over 200 cases, previous cases being used as a control. In the past, treatment in such cases was by irrigations with oxy-cyanide of mercury (1:5,000 to 1:10,000), combined with silver nitrate (1 per cent) used either as drops or by painting, and atropine (1 per cent ointment or drops), in the early and acute stages before the routine painting of the lids. This treatment was undoubtedly beneficial, and alleviated the symptoms in those cases in which there was little corneal involvement. If the cornea was involved, however, even hospitalization with three to four daily treatments did not prevent perforation and its sequelæ in a large proportion of cases, especially those in which the gonococcus was implicated. With the introduction of sulphonamide therapy we did not discard local treatment in cases complicated by secondary infection, but continued this as before. Our primary object, it may be recalled, was to cure these patients, the collection of statistical data for publication being of secondary importance only. We believe that the irrigation has a beneficial effect on the mucopurulent discharge, no matter what other treatment is adopted, and the atropine is indicated as a routine on account of the frequent iritic involvement in these cases. With the addition of sulphonamide therapy to the treatment, a much more rapid response was evident. This was particularly noticeable in a few very chronic cases in which improvement occurred suddenly after prolonged periods of treatment by other methods with no improvement. In the more acute cases, perforation was now seen only occasionally, and its occurrence was restricted to individuals who did not come to hospital until the condition had become well established and perforation was already imminent. Even in cases in which the cornea did perforate, the sequelæ were not so severe if the treatment included sulphonamides.

Numerous workers have recorded that sulphonamides are highly efficacious in the septic ophthalmias. It is not surprising, therefore, to find that it produces a decided clinical improvement in cases of trachoma complicated by bacterial infection; this would result

from alleviation of the latter condition alone. Yet clinically we find that in such cases sulphonamide therapy produces in addition improvement of the trachoma. This usually takes the form of a fairly rapid transition to the stages described as Tr iv or Tr Q. It is impossible from mere clinical observation to determine the mechanism by which this improvement is effected. It may result from a direct action of the drug on the trachoma, but the possibility cannot be excluded that severe secondary infection may, if recovery takes place, cause shedding of the epithelium with scarring, and thus produce an apparent cure of the trachoma.

Spring catarrh.—In cases of trachoma complicated by spring catarrh no rapid improvement in the clinical condition is produced by sulphonamides. Our first series included 4 cases of this nature, and further observation of 15 cases indicates clearly that sulphonamides have no effect on spring catarrh. This is an entirely different type of complication from secondary bacterial infection. It has been regarded as an allergic condition but its aetiology is at present obscure. We are unable to record any definite improvement of the trachoma in these cases.

KERATITIS AND PANNUS

These conditions are considered separately because their aetiology is somewhat uncertain. There has always been some doubt as to whether pannus and keratitis were caused by trachoma *per se*, or whether they were the result of secondary infection. Prior to the introduction of sulphonamide therapy the orthodox view was that pannus was not due to secondary infection but was an integral part of the disease.

However that may be, it is in cases of trachoma with such corneal complications as pannus and keratitis that the most satisfactory results are produced by the use of sulphonamides, both subjectively and objectively. Our first series included nine such cases, in eight of which a very rapid and dramatic improvement was observed, and observations continued during the past two years indicate clearly that this is the type of case in which sulphonamide therapy gives best results. Moreover, perusal of the literature at our disposal in Khartoum indicates that the majority of observers in other countries are in agreement with us on this point; for example, Wilson in Egypt, Lian in the Netherlands East Indies, Loc, Gradle, Richards *et al.*, and Hirschfelder in America, Lugossy in Europe and Hantschek in Iraq. Burnet, Cuénod, Nataf and Roussel have recorded similar results from Tunis with allied compounds; namely, 4:4' diamidino-diphenyl-sulphone glucoside and 'compound 33'—potassium or sodium salt of parnasulphamidophenol—azosalicylic acid. Our own observations have little to add to the descriptions already published of the course in such cases under sulphonamide therapy. Briefly three stages may be described:—

(1) The rapid alleviation of the more immediate subjective symptoms such as pain, lacrimation, photophobia. This usually occurs within a few days.

(2) Resolution of the corneal lesions. This is usually a matter of a few (1 to 4) weeks. The rapidity with which pannus and keratitis may disappear is often remarkable. In mild or early cases the cornea may become perfectly clear. In the more severe cases some haziness may be left, depending on the amount and distribution of the resulting scar tissue; but since the amount of scar tissue deposited depends largely on the duration and severity of the corneal lesions, it is reasonable to believe that, with a method of treatment which promotes such rapid resolution, the formation of scar tissue will be reduced to a minimum. If the cornea is already opaque as the result of previous sclerosis, this, of course, does not disappear during treatment.

With the resolution of the corneal lesions there is usually a striking improvement in visual acuity, which may alter completely the patient's outlook on life.

(3) Improvement of the lids. Exuberant fleshy granulations on the lids tend to disappear fairly rapidly

with the corneal improvement. Complete disappearance of the follicular hypertrophy is another matter. In our experience this is very variable; when it does occur the condition passes into stage Tr iv, but some cases appear to be particularly resistant and reach instead a stage resembling subclinical trachoma, after which treatment seems to have little effect. These cases are practically impossible to follow up properly. After the initial improvement in vision and disappearance of the subjective symptoms the patients rapidly tire of prolonged treatment which, in their opinion, is producing no further improvement; and cease to attend.

Pannus and keratitis are often associated with considerable discomfort and, owing to the permanent damage to vision that they may produce, rank among the most formidable complications of trachoma. In these conditions sulphonamide therapy is infinitely preferable to the prolonged and exceedingly painful methods of treatment previously used.

SUBCLINICAL TRACHOMA

This is a term used locally to designate trachoma in the Sudanese that causes no subjective symptoms, in which vision is unaffected, and which as a rule is only discovered by routine school, military, and other medical examinations. The occurrence of such a condition in the Sudanese suggests that in this race trachoma *per se* is not necessarily a dangerous disease, but its potential danger is due to the diseased eye being less resistant, becoming secondarily infected.

Except for the aforementioned routine examinations we do not see much subclinical trachoma. A series of 15 such cases was treated by sulphonamide, and for comparison a parallel series of 5 cases treated by the routine methods described by McKelvie was selected for observation over the same period. Practically no change in the trachoma could be recorded in either series over a period of four months.

This is in agreement with the findings of Wilson in Egypt, who treated with protosil rubrum 10 children with primary trachoma, and concluded that the drug had no effect on the disease. These cases were seen by one of us (A. R. M.) four months after the commencement of treatment, and they were still undoubtedly cases of Tr i to Tr ii a. Later, Dr. Wilson in a personal communication stated he had used other sulphonamide compounds, with improvement in the congestion, and marked improvement in the pannus cases, but in stage Tr i to stage Tr ii a, there did not seem to be much improvement. Some of these latter cases were also seen by one of us (A. R. M.) who agreed with Dr. Wilson as to the condition present in every case.

The opinions of American workers are divided with regard to the effect of sulphonamides in primary uncomplicated trachoma, but caution is required in the interpretation of the results of different observers. It is uncertain whether the terms used to describe the type of disease are exactly synonymous in all cases, or whether any of the conditions described correspond exactly with subclinical trachoma as observed in the Sudanese. Some of the results, however, are of considerable interest. On the White Mountain Apache Indian Reservation, Forester found that 'the effect of sulphanilamide therapy on early (stage i) trachoma was very striking. Frequently both cornea and conjunctiva returned to normal within the first 10 days'. Thygeson notes that the most rapid response was obtained in cases in which there was no secondary bacterial infection. On the other hand, in the Southern Illinois Trachoma Clinics, Hirschfelder found no definite improvement after two weeks in children 'who had no, or only very slight, subjective symptoms and normal vision', although improvement was noted in other varieties of the disease. Spinning records only 'slight to moderate improvement' in a series of children with chronic trachoma and little or no bulbar or corneal involvement other than slight pannus. Julianelle, Laue, and Whitted conclude that 'in uncomplicated trachoma, improvement measured by

numerical reduction, flattening, and blanching of the follicles is common but genuine recovery is infrequent'.

THE CAUSAL AGENT OF TRACHOMA

Gradle has described the clearing of the cornea and disappearance of the conjunctival follicles in cases of trachoma in which the existence of secondary bacterial infection was excluded by the most exacting methods available, namely, by daily cultures taken from the conjunctiva. MacCallan, on the other hand, maintains that the beneficial effects produced by sulphonamides are entirely due to the elimination of secondary infection, and that the drug has no effect whatever on trachoma.

In the opinion of the present writers it is difficult to see how this vexed question can be satisfactorily settled until it is possible to isolate the causal agent of trachoma and study it experimentally. At the present time it has not even been identified with certainty. From time to time claims have been put forward incriminating one or other of the various bacteria that can be isolated from the conjunctiva, but these have all been discredited for lack of satisfactory evidence. Attention is directed at present to the intracellular bodies described many years ago by Halberstaedter and von Prowazek and now generally known as the Halberstaedter-Prowazek or H. P. bodies. Although definite proof is still lacking, these bodies are now generally regarded as the causal agent of trachoma. Morphologically similar bodies are found in three other diseases, namely, in psittacosis, lymphogranuloma inguinale, and inclusion blennorrhoea. It would appear that with trachoma these three conditions form a special group of virus diseases distinguished by the fact that the virus apparently goes through an elaborate life cycle that can be observed microscopically.

MacCallum and Findlay have shown that sulphonamides can protect mice against the fatal meningo-encephalitis that normally follows intracerebral inoculation of the virus of lymphogranuloma inguinale. Similar results have been recorded by Bär and Levaditi while in the human subject, the drug has been found clinically effective by Gjurić, Kubitzki, and other workers. It was the morphological similarity between the inclusion bodies of lymphogranuloma and the H. P. bodies of trachoma which originally induced the present writers, on the suggestion of Dr. Findlay, to test the effects of sulphonamides in trachoma. In this connection it is of particular interest to note that good results have also been obtained clinically in inclusion blennorrhoea with sulphonamide therapy by McKelvie, Thygeson and other workers. As far as we are aware, no clinical or experimental work has been published describing the effects of sulphonamides in psittacosis, but observations on this point are awaited with some interest.

EFFECTS OF SULPHANILAMIDE ON THE H. P. BODIES

Julianelle, Lane, and Whitted in America, and Burnet, Cuénod, Nataf, and Roussel in Tunis state that one of the effects of sulphonamide is to cause the disappearance of the H. P. bodies from the conjunctival epithelium. Similar findings are reported by Richards, Forster, and Thygeson, who found in addition that the pooled epithelial scrapings taken on the twenty-ninth day from treated patients failed to infect baboons.

In the Sudan it has not been possible to confirm these findings, nor indeed to reach any satisfactory conclusion on this point. It may be noted that the facility with which the H. P. bodies can be demonstrated seems to vary under different conditions, and that their presence is not necessarily associated with active trachoma. Thus Wilson in Egypt found H. P. bodies in 100 per cent of children examined shortly after birth and before clinical trachoma had developed, while at older ages the percentage of positives was much less. A table published by Thygeson and Richards indicates how the percentage of positive findings varies with the stage of the disease in various localities. In the Sudan no figures referring to newly

born children are available to compare with those of Wilson. In older children or adults with recognizable trachoma the proportion of positive findings is rarely as high as 25 per cent in stages Tr i to Tr ii, and under 1 per cent in stages Tr iii.

An attempt has been made to observe the effects of sulphonamides on the H. P. bodies in a series of 20 cases in which the bodies were readily found at the commencement of treatment. The results are as follows:—

Eleven of the patients discontinued treatment as soon as an initial improvement occurred, but before the trachoma had reached a satisfactory clinical condition in which negative scrapings could reasonably be expected. One of these is of some interest. His condition was recorded on 8th January, 1939, as Tr ii to Tr iii, smears positive for H. P. bodies. He was given a course of 28 gm. of sulphonamide over a period of 14 days with considerable improvement. On 21st January, 1939, his condition was recorded as follows: L.E. Tr iii to Q, one or two follicles on tarsus, slide positive for H. P. bodies; R.E. Tr Q, slide negative for H. P. bodies. The patient went away on this date and has not been seen since.

The eyes in three cases were still found positive after treatment had been concluded, and the trachoma had apparently resolved successfully. The patients have not been seen again, so that a follow up has not been possible to determine whether the H. P. bodies disappeared later, or whether relapse took place.

In the remaining six cases the eyes became negative after treatment of varying duration, with apparent cure of the trachoma. Three of these cases were not seen again, but in the other three, positive symptoms were found once more, 14, 21, and 74 days later.

Owing to the small proportion of cases in which H. P. bodies can be found before treatment, negative results after treatment have very doubtful statistical significance in such a small number of cases. Much more significance attaches to the few cases in which the eyes were still positive after treatment, or after becoming negative were later found to be positive. Those few cases indicate that the remarkable clinical amelioration produced by sulphonamides in trachoma is not necessarily associated with the immediate disappearance of the H. P. bodies.

It is doubtful how much significance can be attached to this observation. The persistence or disappearance of the H. P. bodies is probably of no importance as an indication whether the sulphonamides act directly on trachoma or not. The only comparable infection that can be studied under experimental conditions is lymphogranuloma inguinale. MacCallum and Findlay found that sulphonamides were able to protect mice against this infection, which is normally fatal in these animals, but virus bodies were found in the tissues of the treated mice which survived, as well as in the untreated controls, which died. Moreover, in psittacosis it has been shown by Bedson that the virus may persist in the tissues for long periods after natural recovery from the disease, and according to Olitsky and Long this occurs also in a number of other virus infections.

SUMMARY AND CONCLUSIONS

To sum up, sulphonamide therapy has little or no effect in certain cases of trachoma; it produces a variable degree of improvement in others; while in some instances it effects a rapid and very dramatic clinical improvement. In the cases in which it is most effective, sulphonamide therapy is from the patient's point of view infinitely preferable to any other form of treatment that has been used, although it may often with advantage be combined with other forms of treatment.

We have tried to indicate the types of the disease as observed in the Sudan that derive benefit from the drug and those in which the benefit is slight or doubtful since it is evident from the literature that there is some divergence of opinion on this point among workers in different places. In general terms it may be said that the effects of sulphonamide therapy in

trachoma are most dramatic in those cases in which the disease has produced serious clinical manifestations—that is to say, in just those cases in which an effective therapeutic agent is required—whereas in sub-clinical trachoma, in which vision is unaffected, in which the patient has no subjective symptoms and the condition is discovered only by careful clinical examination, sulphonamides appear to have little or no effect. This at least is what we have observed in the Sudan, among a population in which the infection may possibly have been endemic for centuries; it does not follow that these conclusions are applicable in other parts of the world. Moreover our observations (which are here at variance with those of several workers elsewhere) indicate that the rapid clinical improvement induced in the former type of case is not necessarily associated with the immediate disappearance of the H. P. bodies.

The action may be summarized in purely descriptive terms by saying that sulphonamide therapy, without eliminating the infection, enables individuals in whom the infection is pathogenic to deal with it as if it were non-pathogenic. In subclinical trachoma the infection is already non-pathogenic, or only mildly pathogenic, so that the effect of sulphonamide therapy is not so dramatic. This is comparable to the effect observed by MacCallum and Findlay in experimental lymphogranuloma infections; and Browning has recently described in somewhat similar terms the effects of sulphanilamide in streptococcal infections.

It may be emphasized that this conception is purely descriptive and does not explain how the observed effects are produced. MacCallan has attempted to explain it on the assumption that the sulphonamides have no action whatever on trachoma, and the beneficial results observed clinically are entirely due to the effect of the drug on superimposed bacterial infection. This would imply that pannus, keratitis, and the like, indeed all the serious clinical manifestations which react to sulphonamides, are the result of secondary infection, and that trachoma itself is a non-pathogenic or only mildly pathogenic infection of no clinical importance. All the observations recorded in the present paper are quite consistent with this hypothesis, but it is doubtful whether many workers elsewhere will accept this view of trachoma without more conclusive evidence. Probably this question will not be satisfactorily settled until the causal agent of trachoma can be isolated, or at least studied under experimental conditions, like the virus of lymphogranuloma inguinale.

What Causes Flatulence ?

By W. C. ALVAREZ, M.D.

(From the *Journal of the American Medical Association*, Vol. 120, 5th September, 1942, p. 21)

FLATULENCE is one of the commonest symptoms complained of by patients with indigestion or what they think is indigestion. Unfortunately, in many cases the cause cannot be determined. The first thing the physician must do when a patient complains of gas is to find out what he means. Does he mean that he is belching, does he bloat, does he feel as if gas was trapped in a segment of intestine or does he pass excessive amounts of flatus? Curiously a patient may have any or all of these troubles and still not have real flatulent indigestion! The chronic belcher is swallowing air because he is nervous or frightened; the woman who bloats may have only an angioneurotic oedema of her bowel; the man who feels as if he had gas in his stomach may have only a duodenal ulcer or constipation, and the man who is passing much flatus may only be chewing gum and swallowing much air with the saliva.

THE PATHOLOGIC PHYSIOLOGY OF FLATULENCE

Before taking up the clinical aspects of flatulence, I will speak briefly of the mechanisms by which gas gets into and out of the bowel. Contrary to the common

impression, most of the gas is probably not formed through fermentation in the bowel. Analysis have shown that most of it is nitrogen left from swallowed air. Some persons swallow much air, but just why, no one knows. Perhaps when they swallow fluids they do not close their lips over the glass, or in them the muscles of the tongue and nasopharynx behave peculiarly. Every one, of course, swallows some air with 'raised' breadstuffs. Because nitrogen is not easily absorbed from the bowel, nearly all of that which is swallowed in air must go on through to the rectum to be extruded as flatus.

Often, when a person feels that he is distended with gas, roentgenologic examination of the abdomen would show that he is mistaken. In adults there is usually little gas to be seen in the small bowel. What gas there is in the abdomen is generally in the colon. This may be due to the greater ability of the small bowel either to absorb gases or to pass them on rapidly. Some of the gas in the intestine is apparently excreted from the blood. Under the influence of emotion, such excretion can take place with surprising rapidity.

Flatus does not contain much carbon dioxide or oxygen, because these gases are easily and rapidly absorbed by the bowel and thrown out through the lungs. In herbivorous animals large amounts of gas are constantly being taken up by the blood as it passes through the walls of the stomach and cæcum. Obviously, any condition that interferes with the return of venous blood from the intestine is likely to produce gaseous distension. Pneumonia, which interferes with the passage of gases from the lung, can also produce intestinal distension. As Fine has shown, when a man with a bloated abdomen is made to breathe pure oxygen, there is such a steepening of the gradient in nitrogen tension from the intestine through the blood to the alveoli of the lungs that the gas rapidly leaves the distended bowel.

Swallowed air usually is passed through a normal bowel easily and rapidly and painlessly, but gas resulting from the eating of some food to which the patient is allergically sensitive seems often to remain trapped for hours in segments of bowel which are tonically and painfully contracted. Relief comes only when perhaps, with the taking of food, waves again start travelling down the bowel. When the Emperor Claudius, who suffered from flatulence, published an edict that no Roman need feel reticent about passing flatus in public, one of his waggish courtiers suggested that while he was at it he should have passed another law to enable every Roman to pass gas whenever it was distressing him!

BELCHING

An ordinary single 'burp' is due usually to a reverse wave coming up the œsophagus from an overfull stomach, but repeated belching is due always to the swallowing of air. This goes down as far as the cardia and is then returned. Roentgenologic studies show that only occasionally is some of it forced into the stomach. When a man belches repeatedly in this way, it is usually because he is trying to relieve a feeling of distress about the cardia, which I am sure is due often to the running backward of waves on the stomach. He may keep on belching for ten minutes or more, hoping that eventually he will get up one huge belch which will delight him and put an end to his distress. This big belch can be gotten sometimes by drinking a little sodium bicarbonate in water. I think what happens then is that the reverse waves stop running, and the man feels relieved just as he would if an attack of auricular fibrillation was suddenly to stop.

It isn't enough to tell a patient that he is swallowing air and should stop it. To be sure, an intelligent and strong willed person, when he is convinced that he is, in a way, just scratching himself with air and developing a useless and unpleasant habit, will usually stop. But even then the physician should go ahead to find out why the man got to swallowing air. Sometimes it is just a nervous habit, like a tic or the cracking of knuckles which some ignorant persons indulge in when nervous and ill at ease. Many persons belch because

they are so terribly on edge, with the knee jerks exaggerated. Others start belching when they are frightened, perhaps by a feeling that the heart is failing or that some indefinable disaster is impending. Business men may belch at night when they are under great strain and fearful that they are going to crack up nervously.

Many men and women wake in the night frightened, perhaps by an extrasystole, and this starts them to belching. In such cases the main factors are jitteriness and fear of heart trouble, and no treatment can succeed until the patient is reassured. In other cases, and especially with elderly men, the heart is actually failing under the influence of hypertension or coronary disease, and this is what is producing the distress around the cardia. In a few cases the gas that the man is trying to get rid of is in the splenic flexure of the colon. Naturally, then, it cannot be gotten up, no matter how long the man belches. Not infrequently the disease at fault is in the gall-bladder.

Occasionally one finds a particularly expert and noisy belcher who is a near relative of the insane, and his attacks are then due to sudden panicky spells, due perhaps to a fear that he is losing his reason.

BLOATING

When a woman bloats, much can be learned about the cause by questioning her. Has she noticed that the distention follows the eating of any particular foods or does it follow excitement or strain or fatigue? How does the swelling go down? Is gas passed then or isn't it? If no gas is passed, then the bloating is likely to be of the type that is due perhaps to angioneurotic edema of the intestine or an abnormal concentration of blood in the abdomen. In these cases roentgenologic studies show that it is not due to gas in the bowel. Usually this type of bloating is found in a nervous woman who is crossed in love. The swelling increases during the day and generally goes down during the night. With it there may or may not be discomfort, indigestion or constipation. Naturally, in such cases enemas and carminatives do not help. A patient with true bloating due to gas will get relief as soon as the gas is passed.

Curiously, some persons bloat suddenly the minute they drink a glass of water or put any ice cold fluid into an empty stomach. In these cases it would seem that there must be some reflex disturbance which causes gas to pour from the blood into the bowel.

A FALSE FEELING OF FLATUS

A few patients with duodenal ulcer and many with 'pseudo ulcer' will complain not of hunger pain but of a feeling of gaseous distention, which is usually relieved shortly after the taking of food. What happens probably is that the food causes gas to move on out of some segment of the bowel. It starts waves going normally down the intestine. Constipation is a common cause of such distress because the plug in the rectum tends to hold back the waves which would otherwise move the gas onward.

EXCESSIVE FLATUS

Persons with an excessive amount of flatus must be swallowing much air or else they are suffering with much intestinal fermentation or with some breakdown in or reversal of the mechanism by which the blood normally carries gases out of the bowel. In disease these gases can be excreted from the blood into the bowel. Flatus which has no odour is likely to consist of air, while that which is foul is likely to be produced through the fermentation of food. A bad odour can, however, be picked up by the gas as it is churned with faeces and particularly with liquid faeces. Particularly foul flatus is due sometimes to the eating of some food to which the patient is allergic.

CONSTIPATION

Probably one of the commonest causes of flatulence is constipation. The physician should always ask whether the flatulence disappears when the bowels get to moving normally. It helps diagnostically to have

the patient take an enema of a quart of isotonic solution of sodium chloride every day for a few days to see if this works a cure. In some persons the taking of laxatives of any kind will produce flatulence. In case the colon is sensitive, even a small mass of faecal material in the rectum may for hours cause gas to keep forming. That the mechanism at fault is a nervous one is indicated by the fact that the minute the faecal mass is expelled the gas will stop forming.

THE EATING OF CERTAIN FOODS

As Hippocrates noted ages ago, and as the peoples of Europe have discovered during the two world wars, a rough diet can be flatulent and windy. There are many persons with a sensitive bowel who cannot handle much roughage. As this irritates the mucosa, it perhaps interferes with the normal passage of gas out of the bowel, or its presence interferes with the digestion and absorption of carbohydrates. As every one knows, some foods, such as dried beans and cooked cabbage, are particularly likely to produce flatulence. Evidently they contain some chemical substance which irritates the mucosa of the bowel and interferes with the passage of gas through it and into the blood.

Curiously, on questioning 500 patients as to the foods that actually gave them gaseous distress, Hinshaw and I found that most of the persons complained of onions. Next, in order of frequency, the foods most commonly blamed were cooked cabbage, raw apples, radishes, dried beans, cucumbers, milk, fatty or rich foods, melons, cauliflower, chocolate, coffee, lettuce, peanuts, eggs, oranges, tomatoes and strawberries.

FOOD ALLERGY

Probably more commonly than physicians suspect to-day, flatulence is due to the eating of some food or foods to which the patient is allergically sensitive. The result often is abdominal distension and crampy pain. The important point to remember is that some of the worst gas producers are not the notoriously indigestible foods but those such as milk and eggs, which have a fine reputation in the sickroom. Actually, any food can be the offender, and it can be identified and incriminated only with the help of some detective work. Sometimes the patient can discover it by keeping a record of unusual foods eaten a few hours before the bloating appears. Occasionally, some drink such as rum will irritate a sensitive colon and cause flatulence.

OVEREATING

Commonly, an attack of flatulence follows the eating of so much food that the bowel becomes overwhelmed and cannot handle it all. Then some of it ferments and decomposes, and the bowel fills with gas.

ANXIETY OR PAIN

In some persons gas appears rapidly in the bowel under the influence of pain, fear or excitement. Dr. Stafford Warren once pointed out to me that the first film made of a sensitive patient just before he submits to the passage of ureteral catheters usually shows but little gas, whereas the second film, made after the catheters are in place, often shows the small bowel filled with gas.

CHOLECYSTITIS

A common cause of flatulence or bloating or a feeling of flatulence, especially in stout women past middle age, is cholecystitis. Just what the mechanism is which produces the distress is not known. In these cases it often helps if the patient eats less and particularly if she eats a light supper.

COLDS

Some persons with a sensitive bowel suffer from gas when they are coming down with a cold. The virus appears to work some injury to the bowel because often the worst part of the intestinal upset comes during the prodromal period, when as yet there is no disturbance in the nose, throat or lung. Perhaps some mucosal change appears in the bowel before it appears in the nose and throat.

DIARRHOEA

Many persons with diarrhoea are plagued by flatulence, which may be due to a defect in the absorptive functions of the mucosa of the small bowel, related to that which has led to a decrease in the absorption of water and residues from the digestion of foods. Perhaps also the cause of the diarrhoea interferes with the mechanism that causes gas to pass through the mucosa and into the blood vessels of the intestine.

A SENSITIVE COLON

Many patients with a sensitive, mucus forming type of colon suffer with gas. This may form when the patient goes out to dinner or to the theatre, or perhaps when he entertains in his home. The trouble seems to be due partly to excitement and partly to a vicious circle which starts when a little gas forms and cannot, for reasons of politeness, be passed immediately. The distension of the rectum then causes more gas to be formed until the patient is in misery. That the trouble is due to nervous influences is suggested also by the fact that in some persons it can be blocked by the taking of a little paregoric or codeine.

HÆMORRHOIDS

In some few persons flatulence appears to be due to the presence of irritated hæmorrhoids or an inflamed and infected anal ring. The irritation around this ring seems to cause backpressure in the left side of the colon, and this causes gas to accumulate in the splenic flexure. Patients with a large amount of gas in the splenic flexure can secure some relief by getting into the knee-shoulder position or by hanging over the side of the bed so that the gas can rise up into the rectum and from there be expelled.

MILD INTESTINAL OBSTRUCTION

Whenever an older person who has never suffered with flatulence begins to note loud borborygmus, he should immediately have the bowel studied by a good roentgenologist and proctologist. I have seen a number of cases in which borborygmus was the first sign of the development of an obstruction due to a carcinoma of the bowel.

A FAILING HEART

As I have already remarked, especially in older men who have previously been well, the coming of flatulence after exercise, and particularly when the person walks after eating a meal, should make the physician think of a failing heart with some passive congestion in the bowel.

MILD CYCLIC INSANITY

Every so often a woman who comes complaining of gas is found to have a cyclothymic type of personality which causes her to be for a while too energetic and active and then for a while depressed, discouraged, irritable and tired out. She suffers with flatulence during the periods of depression.

INTESTINAL PARASITES

Since one of the possible causes of flatulence is infection of the bowel with parasites such as *Giardia* or *amœbas*, in all puzzling cases of excessive flatus the stools should be examined by an expert.

TREATMENT

From what has gone before, it will be obvious that no one should ever attempt to treat flatulence without first finding out that the patient really has an extra amount of gas in his bowel. If actually there is some indigestion or an abnormal amount of gas present, the next thing to do is to get some idea as to why it is there.

If the flatulence seems to be due to the eating of some irritating food, an effort should be made with the help of a food diary or an elimination diet to find out what it is. The elimination of roughage, raw foods and some of the notoriously gas forming foods and laxatives may help, or the patient may get relief simply by cutting down on the amount of food eaten. The relief of constipation by enemas may give great relief.

Some of the persons who want to belch because they feel that they have gas in the stomach are helped by taking sodium bicarbonate, perhaps with some aromatic carminative added. It is hard to say how much good carminatives do or how they act. Alcohol sometimes works well and peppermint is probably helpful. In bad cases a teaspoon of camphorated tincture of opium often works best. Walking about is sometimes helpful because it starts the gas moving down the bowel. Often the sipping of water or a little milk, or the taking of a little food will help by starting waves running down the intestine. When the gas starts to move out of the segment of intestine in which it has been trapped, the pain goes. When the gas is in the colon, relief can usually be obtained by the taking of an enema. Even when the gas is in the small bowel, an enema may bring relief by removing a plug of faeces which is keeping waves from moving caudally. In some cases a diseased gall-bladder must be removed, and in others a failing heart must be rested.

A friend of mine used to cure belching women by asking them if they were accustomed to pass flatus loudly in public. When, shocked and outraged, they said 'Of course not', he asked why then were they so often passing it noisily by mouth!

Reviews

THORACIC SURGERY.—By Charles W. L. Lester, A.B., M.D., F.A.C.S. 1941. Oxford University Press, London. Pp. vi plus 141. Price, 10s. 8d. Obtainable from Oxford University Press, Bombay and Calcutta

THERE is, characteristically, neither colour nor substance in an outline. One misses most of all in this book the colour that only an account of the author's favourite methods and an evaluation of their results can give.

The substance might have been more carefully selected. The anatomical and physiological sections could well have been omitted; it is difficult to see why the sacrospinalis should have been described in some detail. The rest of these chapters contain elementary points that need no recall to those who have passed an examination in the subjects. As for the remainder of the chapters, the impression left is that much of the

detail of operative methods is irrelevant to the general reader and of slight value to a surgeon.

Finally, the method of printing—the lists of causes, symptoms and signs are very wasteful of space without necessarily making for clarity of expression.

J. M. W.

MENTAL NURSING (SIMPLIFIED).—By O. P. Napier Pearn, M.R.C.S., L.R.C.P., D.P.M. Third Edition. 1942. Baillière, Tindall and Cox, London. Pp. vii plus 332. Illustrated. Price, 6s.

THIS little book is a cram-book for nurses who elect to take the Diploma awarded by the Royal Medico-Psychological Association. That it is now in its third edition would augur that it has fulfilled that service. It has some strange features. One of them is the printing of words like 'anatomy' and 'physiology'



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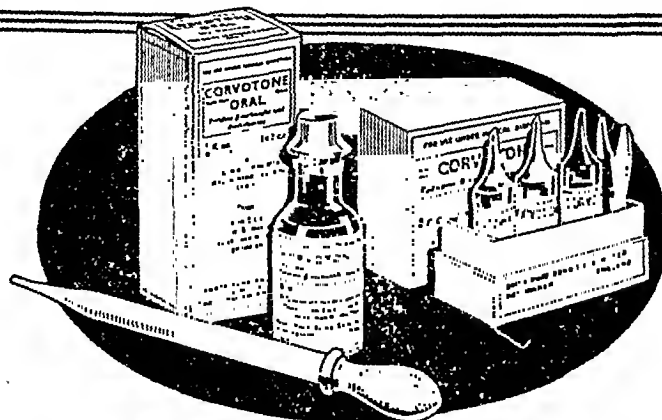
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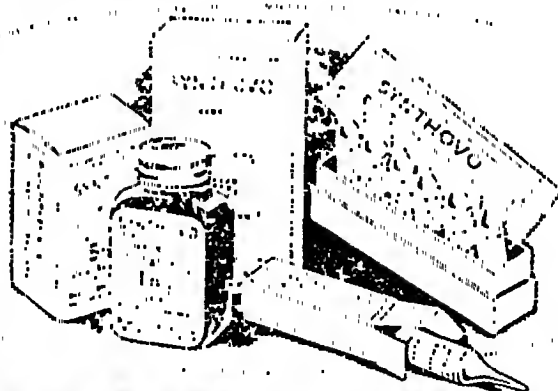
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with hyphens so that they read 'an-at-omy' and 'phys-i-ol-ogy'. The hyphens are in the wrong places. The tone of the book is very chaste. The word 'sex' does not occur in the appendix. In his list of so-called instincts (obviously based on the theories of the late Professor William McDougall) the 'instinct of sex' is referred to as the 'instinct of reproduction'—a very dubious concept. It is not surprising, therefore, to find no reference to any aberration of sex. Another curious feature is the oddity of the illustrations devoted to explain 'instincts'. There is of course no illustration to explain the 'instinct of reproduction'. Indian readers of the book will be amused to learn that the author thinks there is a language called 'Hindoo'. This word may, of course, be a portmanteau expression for Hindi and Urdu.

O. B. H.

PYE'S SURGICAL HANDICRAFT: A MANUAL OF SURGICAL MANIPULATIONS, MINOR SURGERY, AND OTHER MATTERS CONNECTED WITH THE WORK OF SURGICAL DRESSERS, HOUSE SURGEONS, AND PRACTITIONERS.—Edited by Hamilton Bailey, F.R.C.S. (Eng.). Thirteenth Edition. 1942. John Wright and Sons, Limited, Bristol. Pp. x plus 536 with 534 illustrations. Price, 25s.

THAT this work should have reached its thirteenth edition speaks very well for its original author and also for its present editor, under whose guidance new editions have been produced more frequently to meet an increasing demand.

Throughout this book of five hundred odd pages a very high standard is maintained, due probably to the fact that each section is written by an expert and always it is the practical side which is being emphasized.

With such an abundance of sound advice it is almost invidious to pick out any particular section for praise—but those by the editor on the management of abdominal and genito-urinary cases, the sections on surgical thoracic diseases and post-operative pulmonary complications, and the section written by Mr. Gabriel on the rectum, are some that do deserve special mention.

One would have liked to have seen more details about Leriche's injection of local anæsthetic for the treatment of minor orthopædic injuries—similarly more might have been given about transfusion of blood and/or plasma through the sternal bone marrow; and also the treatment of burns of the face and hands might have been dealt with more fully.

In conclusion it only remains for the reviewer to congratulate the publishers on the excellence of their production and to recommend this book very strongly to all house surgeons and to those recently qualified officers now in the Military Services where the guidance of a 'registrar' and an experienced ward Sister is not always readily available.

G. C. T.

MEDICINE. ESSENTIALS FOR PRACTITIONERS AND STUDENTS.—By G. E. Beaumont, M.A., D.M. (Oxon.), F.R.C.P., D.P.H. (Lond.). Fourth Edition. 1942. J. and A. Churchill Limited, London. Pp. xviii plus 801, with 71 illustrations. Price, 28s.

THIS well-known and popular book has now reached its fourth edition. The first edition was published in 1932; it was reprinted twice and once translated into Spanish. The success of the book is undoubtedly due to its distinguished author (the reviewer happened to be his clinical assistant at Brompton) whose knowledge and practical experience of medicine is as great as his teaching ability.

The outstanding features of this book are the presentation of the subject in a compressed form, and its reliability. Most of the sections are packed with a wealth of information presented in a synoptic style. Those on cranial nerves, nephritis and infectious

diseases are particularly good. The illustrations are well chosen and really show what they claim to show. The present volume has been revised and brought up to date with many alterations and additions. The new articles include epidemic catarrhal jaundice, chronic miliary tuberculosis, blast injury of the lungs, prolapsed intervertebral disc, intracranial aneurysm, epidemic myalgia, poison gases, etc. Some of the sections have been largely or entirely re-written. Notes have been added on the Pancoast tumour, primary virus pneumonitis, extra-pleural pneumothorax, x-ray kymography, etc. Other additions include various recent preparations, such as nicotinic acid, sulphaguanidine, picrotoxin, tetanus toxoid and heparin.

The book should prove really very useful to medical students, especially just before their final examinations, also to busy practitioners who wish to refresh their memory quickly.

The author and publishers deserve credit for bringing out a new edition in such difficult times. It is hoped that the present edition will meet with the same reception as the previous ones.

R. N. C.

A POCKET MEDICINE.—By G. E. Beaumont, M.A., D.M. (Oxon.), F.R.C.P., D.P.H. (Lond.). 1942. J. and A. Churchill Limited, London. Pp. vi plus 202. Price, 10s. 6d.

THIS pocket book gives a short account of most of the diseases described in the author's *Essentials of Medicine*. It is meant for students when working in hospital, and while waiting and travelling. It will enable them to review quickly the salient features of the subject before their final examination, and it may also serve as a useful handy reference book for the practitioner's medical bag.

Although much has necessarily been omitted, it is surprising to note that a great deal of valuable matter has been compressed in this small volume of 200 pages. Only the most up-to-date methods of treatment are included with clear-cut and dogmatic statements. We hope it will serve its purpose as a valuable pocket guide.

R. N. C.

SPONTANEOUS AND EXPERIMENTAL LEUKÆMIA IN ANIMALS.—By Julius Engelbreth-Holm, M.D. 1942. Oliver and Boyd, Edinburgh. Pp. xxiii plus 245. Illustrated. Price, 15s.

IN 1932, a trust was founded by the late Sir Dorabji Jamsetji Tata of Bombay, in memory of his wife, the late Lady Tata, C.B.E. Eighty per cent of the income is allocated under normal conditions, in the form of grants or scholarships to workers of any nationality and in any country of the world for research on diseases of the blood with special reference to leukæmia.

The book is an important work on leukæmia in animals and bears 'plentiful evidence of the outstanding contributions made by research workers assisted by the Lady Tata Memorial Trust to the development, by experimental methods, of our present knowledge of the disease'. It is a pity, however, that only 20 per cent of the income is available to the junior Indian workers for scientific research on diverse subjects, and that, up to the present, not one of the senior scholarships has been awarded to an Indian worker, by the Scientific Advisory Committee of the Trust in London.

The author reviews the collective knowledge of spontaneous and experimental leukæmias in animals, and briefly discusses the relationship which these conditions bear to the problem of leukæmia in men. The subject of animal leukæmia is discussed under four different heads, viz, spontaneous leukæmia in animals, transmission experiments in animals, the rôle of heredity in animal leukæmia and lastly attempts to produce leukæmia experimentally in animals.

The infection and tumour theories of leukæmia are next discussed and the author concludes that animal as well as human leukæmias are of the nature of

neoplastic diseases—malignant tumours of the hæmopoietic tissues.

The author justifies the study of leukæmia in animals, since in his opinion 'the results attained are likely to elucidate the corresponding features of leukæmia in man'. For the author has tried to prove that 'leukæmia in animals, especially in mice, is the same disease as leukæmia in man. The peculiar features presented by the disease in some species, especially birds, are more reasonably explained as being due to the special characteristics of the species than to the possibility that fowl leukæmia, for example, is a disease of an entirely different nature from leukæmia in other animals or in man'. But the author will have to substantiate his views with more definite proofs before it can be accepted that leukæmia in animals and man is the same disease.

C. R. D. G.

MODERN DERMATOLOGY AND SYPHILOLOGY.—

By S. William Becker, M.D., and Maximilian E. Obormayer, M.D. 1940. J. B. Lippincott Company, Philadelphia and London. Pp. xii plus 871, with 461 illustrations in text (32 full colour plates). Price, 65s.

The following are extracts from the preface:—

'Dermatology has entered its biologic era. Great strides have been made by studying disease processes rather than the static morphologic pictures of the older dermatology. As a result of this fundamental departure the treatment of many important cutaneous disease complexes have been revolutionized.

An effort has been made to keep the work "modern", in conformity with the title. Methods of diagnosis and treatment that have been largely abandoned or are decreasing in popularity due to introduction of better ones are not given, or are mentioned briefly. This by no means indicates that untried new therapeutic procedures are recommended to the exclusion of old reliable methods.

In an endeavour to make the book a living thing, less stilted and more informal than some textbooks, explanatory material has been incorporated at the beginning of each chapter under "Orientation", in the intimate language of the demonstrator to small groups of students. We hope that this will not only add to the knowledge of the subject, but will enhance interest in the presentations. The subject-matter, too, is presented in the lecture style rather than in the encyclopædic style, which we hope will make it more interesting.

It is our opinion that a textbook should present primarily the ideas and methods of the authors, and secondarily those of other workers. For this reason, the methods of teaching and the therapeutic procedures in use at the University of Chicago Clinics have been emphasized. Since our own method of treating patients with functional dermatoses, while not entirely original, has proved to be of decidedly practical value, it is given in considerable detail.

In order to conserve space, an early chapter is devoted to general considerations of therapy, followed by prescriptions and detailed instruction in preparation and use of medicaments which will give satisfactory results in a high percentage of cases. Therapeutic preparations are arranged alphabetically, so that they may be readily referred to from the various portions of the text where they are recommended. Increasing interest in allergy in various branches of medicine has, we believe, justified inclusion in a special chapter of such concepts of cutaneous allergy as will withstand scientific scrutiny. Growing interest in industrial medicine has inspired us to devote a chapter to the various aspects of dermatoses encountered in occupations.

The reviewer has always objected strongly to the 'static morphological pictures', the hair-splitting differentiation and the stilted nomenclature of the older dermatology. The present book is an excellent example of the modern attempt to bring new life into this old and very conservative branch of medicine. Some doubtful statements are made about some diseases, such as leprosy, of which the authors may have seen but little, but these are minor points. All the important skin diseases of the United States and Europe are well described and discussed and most of them are well illustrated.

These illustrations numbering nearly five hundred are an outstanding feature of the book. Most are half-tone reproductions of photographs and these are excellent; the coloured illustrations number thirty-two and are rather disappointing.

It is unfortunate for doctors in India, that tropical skin diseases rarely seen in the United States are excluded from the book. In spite of this, its value is great.

The last one hundred and ninety pages are devoted to a very thorough and informative discussion of syphilis.

The paper, printing, and the get-up of the book are excellent and there is a very good index.

G. I. I.

J. I.

Abstracts from Reports

TWENTY-SEVENTH ANNUAL REPORT OF ST. DUNSTAN'S, LONDON, FOR YEAR ENDED 31ST MARCH, 1942

Every newly blinded service man and woman should, in the very early days of his or her misfortune, be made acquainted with the contents of Sir Ian Fraser's article in this annual report. It is a message of sympathy and at the same time of inspiration and encouragement. None is better qualified to give advice on blindness than the Chairman of St. Dunstan's, for he was blinded in France in the Great War, and for the past twenty-one years has presided over the activities of that great organization on behalf of blinded service men and women.

'Fear of blindness is the worst part', he writes. 'That was my own recollection of twenty-five years ago, and I confirm it in my dealings with the young men and women of this war. It is a fear of blackness, an economic fear and a fear of loneliness or dependence'. In his very human and understanding message, Sir Ian tells the newly blinded how this fear is dispelled once they become associated with St. Dunstan's.

'The fear of blindness disappears when you see others who have overcome the difficulties', he adds, and then explains how at St. Dunstan's Training Centre, the young men and women mix with men of the Great War who are acting as instructors in braille, typewriting and shorthand, massage, joinery and other handicrafts, and, living in a world of the blind, they, too, quickly begin to concentrate upon the things they can do and to forget the things they cannot do and thus conquer blindness.

'Further', the report goes on, 'old St. Dunstaners of the Great War visit the Training Centre during week-ends and the new men meet these veterans and learn from them at first hand how they have got on. During the course of a few weeks the newcomer meets masseurs, telephone operators, business men, shopkeepers, poultry-farmers, a parson, a lawyer, a salesman, as well as numbers of craftsmen, and he will learn also that men of this war have already passed through their period of training and have gone out into the world to follow the same occupations, or new ones. For instance, more than eighty men—some of the last war and some of

Doctors Remember This Pledge



SWEAR BY APOLLO, the physician, and Aesculapius, and Hygieia, and Panacea and all the gods and all the goddesses — and make them my judges — that this mine oath and this my written engagement I will fulfil as far as power and discernment shall be mine. I will carry out regimen for the benefit of the sick, and I will keep them from harm and wrong... And now, if I shall fulfil this oath and break it not, may the fruits of art and life be mine, may I be honoured of all men for all time; the opposite if I transgress and be foresworn.



Excerpts from the Hippocratic oath, to which physicians have bound themselves since the days of antique Greece
LEFT: AESCULAPIUS RIGHT: HIPPOCRATES



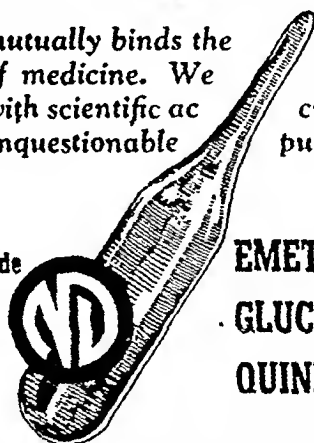
Today, this pledge mutually binds the the manufacturer of medicine. We faith by preparing with scientific accuracy Injectibles of unquestionable

physician and on our part, keep curacy the follow-purity and efficacy :

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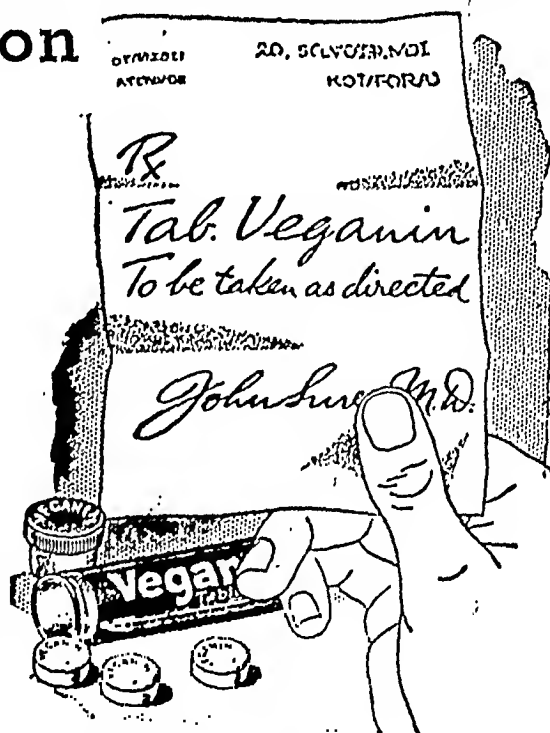
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is assured of relief from pain and its nervous manifestations in a large number of conditions, ranging from simple headache to inoperable carcinoma, with the minimum danger of toxic action.

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Also at Bombay, Madras and Karachi.

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this—are now working in aircraft and munition factories, operating power presses, machines of various kinds, testing, inspecting, packing and so on.

'If you are a newcomer', Sir Ian writes, 'you are amazed at the variety of occupations which are open to the blind. Quickly you learn to read and write and get about by yourself, and soon you choose an occupation and are busy learning it. Almost before you know where you are, you are taking part in the life of the place, enjoying arguments and discussion; playing dominoes, whist or bridge, or you have become a member of a rowing crew, or a tug-of-war team.'

Another section of the report describes the activities of St. Dunstan's in almost every part of the world—how it is functioning there in this war and how the newly-blinded become one of a world family of St. Dunstan's. In the very heart of the enemy's country there is a little St. Dunstan's colony; they are prisoners of war, more than thirty of them, but they are also St. Dunstaners. With the help of the Red Cross and the Y.M.C.A., and the German authorities, St. Dunstan's has established a small school for them and they are learning braille and typewriting and are studying for their future careers.

REPORT OF THE RANCHI EUROPEAN MENTAL HOSPITAL FOR THE PERIOD 1ST APRIL, 1941 TO 31ST MARCH, 1942

THIS hospital admits European patients from many parts of India and provision is also made for ten Indian paying-patients of European habits.

During the period under review the number of patients rose from 254 to 271. The 59 admissions included 3 Italian prisoners, and 1 German internee. There were 10 readmissions. Thirty-seven of the patients are voluntary boarders. The rates of patients cured and improved to daily average strength were 10.46 per cent and 1.78 per cent respectively, and the rates of patients discharged and improved to direct admissions were 31.68 per cent and 3.39 per cent. The death rate was 7.28 per cent.

The report analyses the types of mental diseases treated, by far the largest group being schizophrenia and the second largest being paranoia.

The following are extracts from the report :—

'During the past eight years approximately 25 acres of ground on the hospital lands have been put under cultivation, and the prizes gained for flowers and vegetables have been a source of pride to all concerned. The vegetable garden has continued to show a substantial profit, and to-day it stands the hospital in good stead, for the entire needs of vegetables and flowers are met for the greater part of the year.

The point however that matters most in this hospital is the recovery rate. During the past five years the average ratio per cent of cases discharged as recovered to direct admissions was 37.44. This is an encouraging ratio, but not good enough.

There is a time-worn fallacy that the onset of chronic mental disease is postponed if a patient is allowed to remain in his own home until his behaviour, for social reasons, makes his admission into a mental hospital imperative. There is not the slightest doubt that many early cases are allowed to reach the chronic stage of their illness in this way, in the belief that once they have entered a mental hospital all hope of recovery is lost. This idea is entirely erroneous, and to a great extent, accounts for the low rate of recovery from mental disease.

Take, for instance, schizophrenia, the mystery of psychiatry, which is a more serious problem than either tuberculosis or cancer. In every country where reliable statistics are available, there are more than twice as many hospital cases of schizophrenia as of tuberculosis.

Psychiatrists generally admit that there is an inherent predisposition in the majority of these cases, but it must also be remembered that only a very small percentage of the predisposed develop schizophrenia.

The present war has demonstrated this. Many people who are subjected to physical or mental stress just beyond what they can adequately bear break down.

Experience however shows that it is both unwise and unjust to regard this group as incurable, but it must be stressed that early admission to a mental hospital, far from prejudicing the patient's chances of recovery considerably enhances them.

Although a lot of nonsense is still printed about mental hospitals and their inmates, the public now hold much more rational views, and quite a large number of patients enter the hospital as voluntary boarders.

It is sometimes a very great pleasure to show visitors round the hospital. Many are able to take an intelligent interest, and some officials and public workers admit that they derive inspiration from what they have seen. The majority, however, will see a part of the hospital and then utter the slogan—so well-known to superintendents of mental hospitals—"What you need is a lethal chamber". Since the latter half of 1939 they have been able to vary this with another agreeable formula—"What you need is a well-placed bomb". At one time I myself advocated euthanasia but during more than twenty years of work among sufferers from mental disease, the easy superiority of the eugenicist has completely deserted me. I soon found that I was dealing, not with regrettable accidents, but with people, and uncommonly nice people at that.

In the early part of this year I had an enquiry from an official of the Central Public Works Department requesting me to furnish him with drawings, etc., of "padded cells" but I was in a position to inform him that there were no "padded cells" in this hospital and that their use in the treatment of mental diseases is, fortunately, a relic of the remote past.

Kanke has now its own ARP Controller, Wardens, etc., and everything which a good ARP scheme entails.

Classes of instruction have been arranged, both in English and Hindi, for the First Aid Certificate (St. John Ambulance Association). The classes are being well attended, and some of the members have already qualified for the certificate in First Aid. Arrangements for a course of instruction in ARP by a qualified Instructor have also been made.'

Correspondence

THE TREATMENT OF BACILLARY DYSENTERY

SIR,—There are two points arising from your December editorial on the treatment of acute bacillary dysentery on which I think further comment to be necessary. These are, first, the absorption of sulphapyridine from the gastro-intestinal tract, and second, the mention of chronic bacillary dysentery.

To deal with absorption first: the rate of absorption of the sulphonamides varies directly with their solubility, and they are decreasingly soluble in the order sulphanilamide, sulphathiazole, sulphapyridine and sulphaguanidine. The most readily absorbed—sulphanilamide—reaches its maximum blood concentration about three hours after ingestion; sulphapyridine takes longer. If the patient is suffering from bacillary dysentery, it is easy to imagine the drug in the large bowel after this time. I have been told of a patient with this disease voiding kaolin in his stools three hours after its administration, and I believe that an even more rapid passage through the bowel is possible. It is apparent that in bacillary dysentery the drug is less exposed to absorption than it is in pneumonia; a condition in which there is, in any case, relative bowel stasis. In the instance quoted above, granted the normal passage time for bowel contents to be 18 hours, the possibilities of absorption are reduced sixfold. It is noteworthy that when treating acute bacillary dysentery with sulphapyridine, the incidence of toxic phenomena is

very low. Vomiting, for instance, occurs in less than 2 per cent of patients. This again points to non-absorption of the drug. Further, when the drug is given in full therapeutic doses for diseases other than dysentery, absorption from the bowel is by no means complete. To sum up, it appears to me that the ordinarily accepted mode of action of sulphapyridine is modified by the very nature of bacillary dysentery into one specific for that disease.

The comment I would make on the so-called 'chronic bacillary dysentery' is in the nature of a plea for a more accurate investigation into the etiology of these cases than has hitherto been made, and for their subdivision on this basis for therapeutic purposes. It has always struck me as queer that acute bacillary dysentery, essentially a self-limited disease running its course in 8 or 9 days, should so often become chronic. I have looked the subject up in such books as I have and have only been able to glean very meagre information. All state, with some variation in phraseology: 'Occasionally the chronic form may develop' (this one looks like a textbook heirloom); also that the disease is more common in the inmates of lunatic asylums and in children, and all emphasize the difficulty experienced in isolating the organism from the stools of these patients. Manson-Bahr records that of 107 cases in the Hospital for Tropical Diseases, London, the stools of only three cases yielded positive cultures. Price quotes Cunningham's Indian series in which positive cultures were obtained in 26.7 per cent of cases. It does rather look as if, in the larger proportion of cases, chronic bacillary dysentery is dysentery without the bacilli.

I would therefore like to propose the following hypothesis for the causation of this condition:—

1. Chronic dysentery without bacilli.

This is the type of case in which one finds a thickened tender colon, and on sigmoidoscopy a rigid smooth bowel surfaced with granulations. It is not a chronically infected bowel; but a chronically healing bowel resulting from a severe attack of acute bacillary dysentery. The repair products are being continually swept away by the mechanical action of the faeces and healing is hopelessly impaired. This type of case should respond well to surgical treatment designed to rest the bowel and allowing healing to proceed.

2. Chronic dysentery with bacilli.

As Cunningham's figures indicate, this type is relatively common in this country. On sigmoidoscopy one finds serpiginous ulcers and a pendulous, oedematous, craggy mucosa, pouring pus. I do not think that these cases result from the perpetuation of the original infection in the bowel, but are re-infections either by continued exposure to the original source of infection or by the patient's own person; more frequently the latter I should imagine; it is a common enough process and is well recognized in threadworm infestation where the ova lodge and even develop in the warm natal clefts. It should be borne in mind that chronic bacillary dysentery occurs more frequently in lunatics, children and primitive societies. These are all types in which one can presuppose the absence of a conscientious personal hygiene.

That these theories of coprophagic reinfection and impairment of the healing process are probably correct is witnessed by an observation made in an article abstracted by you in the same number of the *Gazette* (Lyon: Chemotherapy in Acute Bacillary Dysentery). He states: 'Sulphaguanidine was not quite so effective in the recurrent attacks of bacillary dysentery and in the more chronic forms. If, however, the stools were bloody or contained pus, or if the culture demonstrated that they contained dysentery bacilli, the results were generally good'. Thus, if chemotherapy is not to be discredited in chronic bacillary dysentery, it must not be empirically used, but with due regard to the presence or absence of an active bowel infection.

D. J. LAPPING.

PANITOLA P. O.,
UPPER ASSAM,
20th January, 1943.

TREATMENT OF LOCAL SORE

SIR,—It has always been the task of Ayurvedic and Unani jarnahs (surgeons) to treat the local sore and they are doing it with commendable success. Observations and experience amply prove that the indigenous treatment of this sore is very effective, cheap and quick.

The allopathic treatment of to-day with carbon dioxide snow is a very lengthy treatment. In practice, I find that the sore takes a long time to heal and the treatment is also very painful. Moreover, it leaves a scar which to a certain extent disfigures the skin. A carbon-dioxide cylinder and a press have to be kept, and I found that the treatment could not be given without the help of an assistant. Further, neither formerly nor now it is accessible to the outdoor rural dispensaries, with the result that the patients residing in villages and the suburbs cannot avail themselves of this treatment.

Local treatment of the sore with tartar-emetic and quinine sulphate ointment, each 5 per cent, has also proved to be painful enough to scare away the patients.

Local treatment with cignolin, 60 gr., zinc oxide 240 gr., olive oil 240 minims was applied as a paste, but it took a very long time to heal the sore. Moreover, a few patients touched their eyes and got sore eyes. The paste cannot be applied on the face, due to cignolin.

Treating the local sore by berberine sulphate injections is painful and this requires three to four injections for one local sore. Thus, it takes at least four to five weeks and is costly. Moreover the treatment cannot freely be administered to the public at large.

Antimony compound injections, such as neostibosan and foundin and other antimony compounds were also used by me during my practice. At least four to five injections have to be given intravenously, one injection every day, without a break. The sore did heal, but it took two to three months. This too never found favour with the patients.

Atebrin injections were found successful, but had to be given up due to the scarcity of the drug.

A new and efficient treatment which I have been able to find out, as a result of long experience, is given below.

The treatment is cheap and does not require much skill. Being without complications, it can be tried easily by the rural dispensaries as well.

The sore is cleaned up well. Scabs, crust, etc., are removed by a starch poultice. This cleaning may be done mechanically. When the wound is quite clean, a very small quantity of mercury oxycyanide is sprinkled all over the sore and a little beyond all round. It is then dressed with ointment on cotton-wool. The dressing is kept for twenty-four hours, and the slough, if any, is removed. The dressing is changed every three to four days.

The ointment used for dressings is as follows:—

Fuchsin
Gentian violet
Brilliant green as 5 per cent solution in alcohol.	3i
Hydrargyri ammoniata	5 gr.
Cod-liver oil	3i
Vaseline	3i

This is found to be not only inexpensive but a swift and sure cure. It hardly takes three to four dressings and is not at all painful. Should the mercury oxycyanide application in sensitive cases cause pain, one per cent porcein powder may be mixed with it. This will relieve whatever little pain is felt.

W. GUPTA.

53, PUNCH KUIN ROAD,
NEW DELHI,
7th January, 1943.

"THE MOST EFFECTIVE STIMULANT"

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In 1911, the late Professor Thompson, of Dublin, established that Bovril had the power of ministering to nutrition by the assistance it gave to the assimilation of other foods. Recently a remarkable series of experiments has been conducted at an English University. A group of medical students volunteered to undergo the unpleasant experience of allowing the passage of an œsophageal tube into the stomach so that accurate studies might be made of the effect of certain beef preparations. One of the substances investigated was Bovril.

As a result of these experiments (described in detail in the *British Medical Journal* of August 28th, 1937) Bovril emerged as 'the most effective stimulant.' Briefly, it was proved that Bovril increased the supply of gastric juices where there was a deficiency and restored it to normal. It is an accepted medical fact that people of sedentary habits generally suffer from a lowering of the essential gastric activity; Bovril rectifies this and, by facilitating the digestion of proteins, enables full nourishment to be gained.

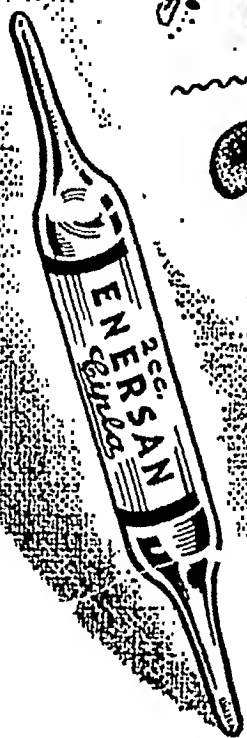
Everyone, therefore, who is run down through strain or illness, or who feels in need of extra strength to cope with the demands of modern life, should take a cup of hot Bovril daily. It is a delicious and stimulating way of keeping fit and strong.

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Service Notes

APPOINTMENTS AND TRANSFERS

LIEUTENANT-COLONEL D. P. MACDONALD, M.C., I.M.S. (Retd.), is appointed Director of Production (Instruments and Appliances) in the office of the Director-General, Indian Medical Service, with effect from the 9th December, 1942.

Major G. Milne, an Agency Surgeon, is appointed as Agency Surgeon in Bundelkhand, with effect from the afternoon of the 10th December, 1942.

INDIAN LAND FORCES

(Emergency Commissions)

To be Captain

Manuel Joseph Saldanha. Dated 2nd October, 1942.

To be Lieutenants

Eugene Eustace LeFeuvre. Dated 5th April, 1942.

Nirmal Parkash. Dated 6th December, 1942.

Madhusudan Vishnu Bapat. Dated 2nd November, 1942.

Gajanan Sadashiv Marathe. Dated 11th November, 1942.

Manoranjan Dutt. Dated 18th November, 1942.

Himangshu Kumar Das. Dated 18th November, 1942.

Amalendu Das Gupta. Dated 26th November, 1942.

Gunindra Nath Sen Gupta. Dated 28th November, 1942.

Andrew Kenneth Sear. Dated 30th November, 1942.

Syed Abdul Majid. Dated 1st December, 1942.

2nd December, 1942

Sourindra Mohan Ghosh. Radhikaranjan Roy.

4th December, 1942

Bhupendra Patra. Sasanka Mohan Bhatta-

Bireswar Ghosh. charjee.

Prabhanjan Deb. Alfred Edward Fraser-

E. Bheemasankaran. Smith.

Panchugopal Basu. Walter Barr Johnston.

5th December, 1942

Krishnaswamy Gajjala. Kitanginathu Cherian

Vadivelu Chittor. Koshy.

Nanna Somaraju. Sulochan Ghosh.

Kombra Bail Ratnakar. Arthur Stanley Reilly.

Rao. Chenpuzha Neelakandan

Albert William Sundara- Narayana Mimbisan.

nathan. Mettu Ranga Reddy.

Satyendra Nath Mitra.

6th December, 1942

M. R. Gopalaratnam.

Sundaraja Somasundaram.

Venkataswamy Parthasarathy Naidu.

A. Kumhikrishna Nambiar.

Satya Ranjan Paul.

7th December, 1942

K. R. Venkatachalapathy. Basant Krishnan Vaid.

Esmond Joseph Frederick. Dated 8th December, 1942.

10th December, 1942

Prem Chandra. Naresh Chandra Talpatra.

13th December, 1942

Jerome Francis Guerra. Colin Thomas Symonds.

Stuart Everard Tanner. Dated 15th December, 1942.

Pankaj Kumar Bancrjec. Dated 16th December, 1942.

To be Lieutenants (on probation)

Jean Mackenzie Rae Mason Johnson. Dated 18th June, 1942.

Nora Kathleen Woll. Dated 29th September, 1942.

Gwendolen Mary Higgins. Dated 29th September, 1942.

(WITHIN INDIAN LIMITS)

To be Lieutenants

Rama Krishna. Dated 13th November, 1942.

Sudhir Kumar Das. Dated 4th December, 1942.

Mohd. Khan Tukhi. Dated 5th December, 1942.

G. I. Ramachandranan. Dated 8th December, 1942.

Parimal Chandra Das Gupta. Dated 6th December, 1942.

Sudhansu Kumar Mozumdar. Dated 16th December, 1942.

To be Lieutenants for service in the Indian Air Force

Hardial Singh Gill. Dated 24th November, 1942.

Harendra Nath Dutta. Dated 27th November, 1942.

Oyitti Manakadan Satyendran. Dated 5th December, 1942.

Santosh Kumar Das. Dated 8th December, 1942.

Kunhinni Nair Kothaneth. Dated 12th December, 1942.

INDIAN MEDICAL SERVICE (DENTAL BRANCH)

(Emergency Commissions)

To be Lieutenants (on probation)

2nd October, 1942

Kartar Singh. Kiran Chandra Chatterjee.

Anand Kumar Madhok. Dated 5th October, 1942.

Mohmood Hayat Khan Saljuky. Dated 9th October, 1942.

PROMOTIONS

INDIAN LAND FORCES

(Emergency Commissions)

Captains to be Majors

23rd October, 1942

S. D. Dalal.

Z. H. Khan.

M. N. Rajan.

V. A. Belsare.

S. N. Kaul.

A. N. Malhotra.

C. V. Ramchandani.

T. S. Uveroi.

C. Bhola.

C. M. Kikani.

P. L. Burman.

R. Mansoor.

K. C. Varma.

C. V. Krishnaswami.

L. Oswald.

A. K. Nandi.

P. K. Gupta.

R. Kasliwal.

Sris Chandra Ray.

D. G. Karandikar.

J. N. Choksy.

K. N. Tandon.

M. N. Khanna.

M. S. Bazaz.

M. S. Babbar. Dated 23rd October, 1942.

W. M. D'Souza. Dated 24th December, 1942.

Lieutenants to be Captains

11th May, 1942

G. R. Butterfield. A. C. Grecne.

G. Barwell. Dated 10th July, 1942.

J. T. Prendiville. Dated 28th July, 1942.

M. A. C. MacHugh. Dated 10th August, 1942.

W. M. Doolin. Dated 26th August, 1942.

C. Sonick. Dated 22nd September, 1942.

J. M. Mungavin. Dated 11th May, 1942.

J. M. Drury-White. Dated 20th September, 1942.

H. Singh. Dated 29th August, 1942.

M. Bhanu. Dated 2nd October, 1942.

I. A. Khan. Dated 5th November, 1942.

K. P. A. Khader. Dated 5th November, 1942.

H. N. Roy. Dated 6th November, 1942.

B. L. Silveira. Dated 7th November, 1942.

N. G. Kendaswamy. Dated 28th December, 1942.

S. C. Pinto. Dated 5th August, 1942.

M. H. Collins. Dated 2nd September, 1942.

G. E. Aling. Dated 29th September, 1942.

2nd October, 1942

A. K. Choudhuri.

C. Venkateswarlu.

C. P. Nair.

P. K. Chandrasekharan.

C. M. Sundarajan.

P. K. Basu.

A. K. Basu.

3rd October, 1942

M. D. R. Naidu.

V. M. Husain.

5th November, 1942

T. R. Seshadri. P. L. Karney.

6th November, 1942

M. Raskino. B. R. Sengupta.
 R. F. Noronha. D. A. Punolik.
 M. M. Bhattacharyya. C. S. P. Sharma.
 B. N. Banerjee. A. C. Basu.
 B. Sarkar.

7th November, 1942

R. Prasad. N. I. Sreenivasan.
 L. E. Chaves. Dated 10th November, 1942.
 A. S. Reddy. Dated 10th December, 1942.

*(Emergency Commissions)**Lieutenants to be Captains*

M. R. Dhamdhare. Dated 1st December, 1942.
 D. Bhatt. Dated 3rd December, 1942.

18th December, 1942

M. Y. Ghaznavi. S. K. Mukherjee.
 S. P. Mehta. H. L. Chhabra.

19th December, 1942

J. S. Sarkaria. N. S. Khan.

26th December, 1942

L. M. Hogg. T. L. W. McCullagh.

28th December, 1942

C. Muthukrishnan. S. Zacharias.
 M. V. Kurian. V. Gnanadikham.
 E. S. Linton.
 P. P. Paulose. Dated 29th December, 1942.

Lieutenants (on probation) to be Captains (on probation)

K. P. G. Menon. Dated 10th July, 1942.
 M. Sen. Dated 7th August, 1942.
 E. A. Beetles. Dated 15th August, 1942.

4th September, 1942

R. I. Krishnaswamy. B. V. Rao.
 K. E. R. Robertson.
 G. S. Majumdar. Dated 7th September, 1942.
 M. K. Mitra. Dated 27th August, 1942.
 B. E. Pardiwalla. Dated 1st October, 1942.
 A. Sayeed. Dated 1st October, 1942.
 M. Ahmad. Dated 8th October, 1942.
 R. B. More. Dated 15th October, 1942.
 C. Suryanarayana. Dated 23rd October, 1942.
 A. Haq. Dated 25th October, 1942.
 S. G. Sidenur. Dated 25th October, 1942.
 C. J. Pinto. Dated 1st November, 1942.
 A. Rashid. Dated 3rd November, 1942.
 H. R. Ohrie. Dated 10th November, 1942.
 N. A. Subramanyam. Dated 11th November, 1942.
 D. C. Bhar. Dated 16th November, 1942.
 M. Banerjee. Dated 30th November, 1942.
 K. Sha. Dated 15th December, 1942.
 A. K. Bose. Dated 15th December, 1942.
 S. P. Subramaniam. Dated 21st December, 1942.
 T. M. Mathew. Dated 24th December, 1942.
 J. R. Pereira. Dated 25th December, 1942.
 M. Amin. Dated 28th December, 1942.
 Z. M. Pandher. Dated 30th December, 1942.

*(WITHIN INDIAN LIMITS)**Lieutenants to be Captains*

2nd October, 1942

P. K. Paul. P. O. Kuriappen.
 L. M. Banerjee. K. C. Ghosh.

3rd October, 1942

T. D. Saraswaty. C. G. P. Rao.
 S. A. Rahim.

4th October, 1942

R. C. Chakravarti. S. M. Qoreishy.

5th October, 1942

N. B. D. Gupta. P. S. Anantharaman.
 S. K. Kelkar. Dated 10th October, 1942.

5th November, 1942

M. S. Narayanan. L. Narayan.

6th November, 1942

P. K. Sen. H. Reza.
 M. R. Juneja. H. B. Das.
 A. J. Rebeiro.

8th November, 1942

K. S. Kalra. M. I. Venkateswaran.
 N. Choudhury. Dated 9th November, 1942.
 S. P. Iyer. Dated 12th November, 1942.
 P. R. Solanki. Dated 15th November, 1942.

RETIREMENT

Lieutenant-Colonel M. M. Khan. Dated 16th October, 1942.

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Original Articles

THE TREATMENT OF KALA-AZAR WITH DIAMIDINO-DI-PHENOXY-PENTANE. PRELIMINARY OBSERVATIONS ON THE TREATMENT OF 32 CASES

By L. EVERARD NAPIER, C.I.E., F.R.C.P. (Lond.)

and

P. C. SEN GUPTA, M.R. (Cal.)

School of Tropical Medicine, Calcutta

DIAMIDINO-DI-PHENOXY-PENTANE is one of the aromatic diamidines synthesized by Ewins in 1939 and found to have a curative action in *Trypanosoma rhodesiense* infection in rabbits and *Babesia canis* infection in puppies by Lourie and Yorke (1939). This compound was successfully used in a small number of cases of visceral leishmaniasis in man by Kirk and MacDonald (1940), Kirk and Sati (1940) and Adams (1941). Humphreys (1942) also used it in two cases of oro-pharyngeal leishmaniasis, with successful results. It has been found to be satisfactory in the treatment of sleeping sickness by Saunders (1941).

Adler and Tchernomoretz (1942) tested the therapeutic activity of this compound in Syrian hamsters infected with *Leishmania donovani*, and found that repeated injections of 3 to 5 mg. per kilo of body-weight controlled a light infection, but for heavier infections 20 mg. per kilo was not as effective as 2 mg. of diamidino-stilbene.

The drug was received by us about the middle of last year and up to now we have treated thirty odd cases. The immediate results of treatment in the first thirty-two cases are given below; this will give an idea as to its value as an anti-kala-azar drug in India.

All the patients of this series were admitted for treatment in the hospital of the Calcutta School of Tropical Medicine. Twenty-eight of these patients were Indians and four Anglo-Indians; twenty-six were males and six females.

Age.—The age distribution was as follows:—

1 to 10 years	..	10 patients
11 to 20 "	..	8 "
21 to 30 "	..	12 "
31 to 40 "	..	2 "

TOTAL .. 32 patients

The duration of illness varied from less than one month to two years and the mean was 7.09.

Diagnosis.—The diagnosis was confirmed in all cases but one (case 21) by the demonstration of *Leishmania donovani* in the spleen or sternal puncture smear. In case 21, the aldehyde test was strongly positive and the patient had cancrum oris; the diagnosis was therefore certainly kala-azar and as treatment was urgently indicated it was commenced immediately on admission.

Blood picture before treatment.—A full blood count was done in all cases on admission and at least once more before the patients were discharged from the hospital. In the few cases in which the patients left hospital against advice, the second blood count was omitted; also in one fatal case it was not done. The hæmatological investigations were carried out according to the methods described in *Hæmatological Technique* by Napier and Das Gupta (1941).

The following tables I and II give the frequency distribution of the hæmoglobin values and total leucocyte counts in this series of cases:—

TABLE I
Hæmoglobin level

Grammes of Hb. per 100 c.mm. of blood	Cases before treatment	Cases after treatment
3.1- 4.0	2	..
4.1- 5.0	2	..
5.1- 6.0	4	..
6.1- 7.0	13	..
7.1- 8.0	2	1
8.1- 9.0	4	4
9.1-10.0	4	1
10.1-11.0	0	12
11.1-12.0	0	4
12.1-13.0	1	5
TOTAL	32	27
Mean \pm standard deviation	6.591 \pm 1.549	10.573 \pm 1.38

TABLE II
Leucocyte counts

Range of leucocyte count in thousand per c.mm.	Cases before treatment	Cases after treatment
1.1- 2.0	16	..
2.1- 3.0	4	..
3.1- 4.0	8	6
4.1- 5.0	1	2
5.1- 6.0	1	5
6.1- 7.0	0	4
7.1- 8.0	2	2
8.1- 9.0	..	4
9.1-10.0	..	2
10.1-11.0	..	1
11.1-12.0	..	1
TOTAL	32	27
Mean \pm standard deviation	2.718 \pm 1.52 thousands	6.43 \pm 2.35 thousands

It will be seen that the hæmoglobin per cent was between 5 and 10 grammes in 27 out of 32 cases: the mean was 6.591 \pm 1.549 g. per 100 c.cm. of blood. The leucocyte counts showed a mean of

2.718 \pm 1.52 thousand per c.mm. (The tables also give the values after treatment; these will be referred to later.)

Treatment.—The cases have been classified into two groups: one group, the 'ordinary' cases, in which no treatment, or only an inefficient course of treatment, had been given; and the 'resistant' cases, in which an ordinarily efficient course of treatment had failed to effect a cure, or which showed relapse after a full course of treatment. Additional details regarding the resistant cases are given in protocol II. Generally, the cases which fail to respond to, or relapse after, 10 to 12 injections of neostibosan or urea-stibamine, or a full course of 10 injections of diamidino-stilbene, are regarded as 'resistant'.

In all except three cases (cases 3, 4 and 10) diamidino-di-phenoxy-pentane was the only specific drug used. In these three cases we had previously given a course of injections of sodium antimony gluconate with no effect in case 4, and slight improvement but not cure in the other two.

We have not placed these cases in the category of 'resistant' cases, as the drug used cannot be regarded as possessing anti-kala-azar activity comparable to neostibosan and urea stibamine, and one course of injections of this compound cannot be regarded as an 'ordinarily efficient' treatment.

Besides the specific treatment, complications such as pneumonia (two cases) and bacillary dysentery (two cases) were treated successfully with sulphapyridine and sulphaguanidine, respectively, and other minor complications, such as epistaxis, bronchitis, diarrhoea, etc., were treated symptomatically. The course of treatment with M.&B. 800 (diamidino-di-phenoxy-pentane) was followed after about a fortnight by a course of cinchona febrifuge in most cases, to eradicate any latent malarial infection. The treatment of helminthic infection, if present, was postponed to a date well after the completion of the course of M.&B. 800. In a few cases, hæmaturinics were administered to bring up the hæmoglobin level to the 'normal'.

The drug was administered in every instance by the intravenous route; 1 per cent solution in fresh sterile distilled water was used. The injections were given daily and usually about three hours after a light meal. In the patients with a resting systolic blood pressure below 100 mm. of mercury, an injection of adrenaline (1 in 1,000) 0.25 c.cm. was given hypodermically before the administration of M.&B. 800.

Dosage.—In adults, the dosage adopted was usually 0.025 g. for the first injection, 0.05 g. for the second, 0.075 g. for the third, and then by daily increase of about 15 to 20 mg. the maximum dosage of 1 mg. per pound of body-weight was reached, and this dose was continued until the end of the course. In children, somewhat smaller initial doses were given, and the maximum was reached by small increases of 5 to 10 mg.

We made no attempt to use a standard total dose for every patient, but used the drug on the dosage scheme mentioned above, giving usually 10 injections in 'ordinary' cases and 12 to 15 injections in 'resistant' cases. The number of injections given to the various patients is given in table III.

Whenever any patient showed any untoward reaction to the drug, we either repeated the previous dose or gave adrenaline previous to the injection of the drug.

TABLE III
Number of injections

Number of doses	Ordinary cases	Resistant cases
6	1	0
9	0	1
10	15	0
12	3	7
5 + 10	0	1
10 + 10	1	1
12 + 10	0	1
12 + 12	0	1
TOTAL	20	12

The total dosage and the relative dosage per 100 lb. per body-weight, for the two groups of cases, 'ordinary' and 'resistant', are given in tables IV and V. The dosage in one fatal case (case 2) is omitted from the analysis as this patient was given only two injections.

TABLE IV
Total dosage

Range in grammes	Ordinary	Resistant
0.11-0.20	1	..
0.21-0.30	1	2
0.31-0.40	3	2
0.41-0.50	2	1
0.51-0.60	1	0
0.61-0.70	2	0
0.71-0.80	3	1
0.81-0.90	4	1
0.91-1.00	1	1
1.01-1.10	0	1
1.11-1.20	1	1
1.21-1.30	0	0
1.31-1.40	0	0
1.41-1.50	1	0
1.51-1.60	0	0
1.61-1.70	0	0
1.71-1.80	0	0
1.81-1.90	0	0
1.91-2.00	0	1
TOTAL	20	11

The mean total dosage for the 'ordinary' cases works out at 0.670 \pm 0.318 g., and that for 'resistant' cases at 0.760 \pm 0.138 g. As regards the relative total dose, i.e., the total

dose per 100 lb. of body-weight, the mean is 0.895 ± 0.226 g. for ordinary cases and 1.259 ± 0.454 g. for resistant cases. These values have been compared with the corresponding dosages of diamidino-stilbene (Napier, Sen

TABLE V

Relative total dosage per 100 lb. of body-weight

Range in grammes	Ordinary	Resistant
0.41-0.50	1	..
0.51-0.60	0	..
0.61-0.70	1	1
0.71-0.80	1	0
0.81-0.90	11	0
0.91-1.00	3	1
1.01-1.10	1	3
1.11-1.20	1	2
1.21-1.30	0	1
1.31-1.40	0	1
1.41-1.50	0	..
1.51-1.60	0	..
1.61-1.70	0	..
1.71-1.80	1	..
1.81-1.90	0	..
1.91-2.00	0	..
2.01-2.10	..	1
2.11-2.20	..	1
TOTAL	20	11

Gupta and Sen, 1942), and have been found not to be significantly different from those of the diamidino-stilbene series.

Immediate reactions

The immediate reactions to the injections of diamidino-di-phenoxy-pentane were similar to, but very much milder in degree than, those occurring after diamidino-stilbene. The patients usually complained of a burning sensation or a sensation of warmth in the abdomen, face and chest, soon after the injection. This disappeared in the course of the next three to five minutes. Other symptoms complained of were transient giddiness, nausea, and vomiting when the injection was given on a full stomach, and some sweating. In no case did the alarming symptoms, breathlessness, severe palpitations, profuse sweating, and collapse, occur. The fall of blood pressure that has been noticed after the administration of this compound is relatively slight compared with that seen after diamidino-stilbene.

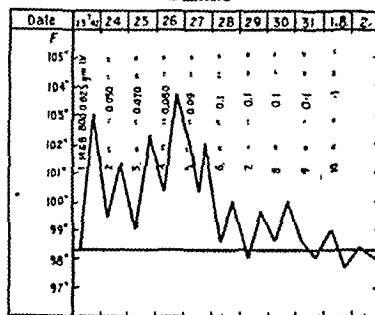
No other untoward reaction, immediate or delayed, and no case of any condition like what we might call 'post-diamidino-stilbene neuropathy' (Napier and Sen Gupta, 1942) has so far been encountered. In one fatal case (case 2), the patient, who was gravely ill, developed thrombocytopenia, purpura and jaundice with hæmorrhage from the bowels and under the skin, after receiving only two doses of the drug. It is unlikely that the administration of two small doses of this drug led to these complications. Untreated cases of kala-azar are known

to develop complications characterized by similar hæmorrhages.

Results of treatment

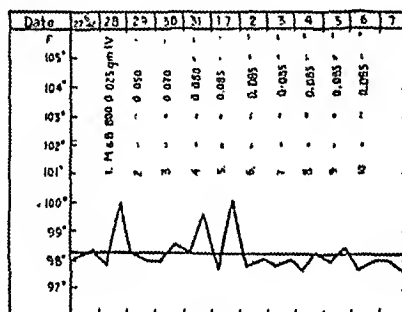
Fever.—In most cases the fever dropped to normal about the end of the course of injections: in a few cases it came down earlier, i.e., after the fifth to the seventh injection. In some cases, the fever came down to normal 2 to 4 days after the whole course of injections had been completed. A small number of cases were afebrile before they commenced treatment. These patients had attacks of intermittent fever for

CHART



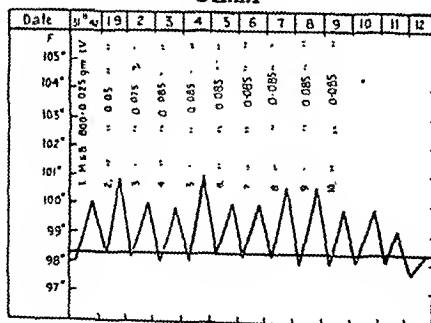
Case 1

CHART



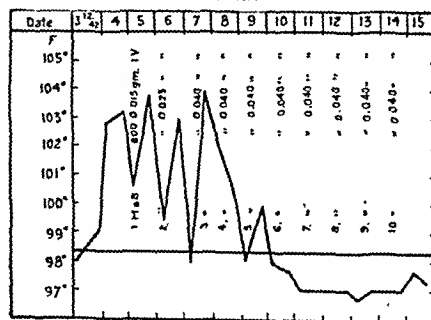
Case 3

CHART



Case 13

CHART



Case 27

PROTOCOL
Summary of cases treated with

Serial number	1	2	3	4	5	6R	7	8	9	10R
Race	Ind.	Ind.	Ind.	Ind.	Ind.	Ind.	Ind.	A.-I.	A.-I.	Ind.
Age in years	30	14	25	3	18	10	28	19	23	21
Sex	M.	M.	M.	M.	F.	M.	M.	M.	M.	M.
Weight in pounds	96	79	83	22	72	44	82	101	133	75
Duration in months	5	1	18	(1)	10	12	2	1	3	18
Spleen, inches below cost. marg.	5	5	3½	1	6½	6	4½	3½	3	7
Hæmoglobin gm. per 100 c.cm.	6.87	7.7	8.93	6.3	6.18	6.46	8.93	12.1	9.625	7.42
Leucocytes per c.mm. in 10³ ..	1.55	3.20	3.75	7.5	1.8	3.1	1.8	2.6	2.1	1.2
Diagnostic puncture—spleen or sternum.	+	+	+	+	+	+	+	+	+	+
Total dose M.&B. 800 (grammes)	0.815	0.670	0.735	0.22	0.625	0.305	0.705	0.805	0.930	0.285
Total dose per 100 pounds of body-weight, g.	0.848	0.848	0.885	1.00	0.868	0.693	0.859	0.797	0.699	0.675
Number of doses	10	10	10	12	10	9	10	10	10	5
Final hæmoglobin, g.	10.72	10.31	12.375	10.03	8.66	..	12.375	..	13.2	10.312
Final leucocyte count	4.0	5.5	9.8	8.6	3.6	..	6.0	..	7.0	10.5
Final spleen, inches	R.	2	R.	O.	3	..	P.	..	O.	2½
Final weight, lb.	103	84	91	(24)	77	..	87	..	147	90
Immediate result	C.	C.	C.	C.	C.	D.	C.	D./O.	C.	C.

PROTOCOL I—concl'd.

Serial number	24	25	26	27	28	29R	30	31R	32R
Race	Ind.	Ind.	Ind.	Ind.	Ind.	A.-I.	A.-I.	Ind.	Ind.
Age in years	26	5	3	8	30	7	27	17	20
Sex	M.	M.	M.	M.	M.	F.	F.	M.	M.
Weight in pounds	83	33	20	40	97	38/37	88	104	81
Duration in months	3	½	6	12	24	9	4	24	10
Spleen, inches below cost. marg.	3½	2	1	1½	7	7	5½	6½	5½
Hæmoglobin gm. per 100 c.cm.	4.1	4.95	9.9	7.012	8.52	5.08	5.77	5.6	6.73
Leucocytes per c.mm. in 10³ ..	1.3	5.1	3.1	3.4	3.4	1.55	1.2	2.2	1.6
Diagnostic puncture—spleen or sternum.	+	+	+	+	+	+	+	+	+
Total dose M.&B. 800 (grammes)	0.740	0.305	0.185	0.360	0.815	0.420	0.415	1.040	0.865
Total dose per 100 pounds of body-weight, g.	0.740	0.924	0.925	0.90	0.840	0.355	0.471	1.00	1.067
Number of doses	10	10	10	10	10	12	6	12	12
Final hæmoglobin, g.	7.56	10.31	12.375	8.52	10.72	8.9	10.72	9.075	..
Final leucocyte count	3.3	8.85	8.0	9.25	4.3	4.0	3.7	6.1	..
Final spleen, inches	3½	R.	R.	P.	3	4	R.	R.	..
Final weight, lb.	86	31*	24½	44	108	41	93	103	..
Immediate result	Not cured.	C.	C.	C.	C.	C.	C.	C.	C.†

* Due to loss of anasarca.

† Subsequently known to be doing well.

some days during the specific treatment and, towards the termination of the course, they became apyrexial again.

Spleen.—In most cases the size of the spleen was quite unaffected during the course of injections and for about a week after it. Then it gradually became softer, flatter and more mobile, and progressively decreased in size. In a few cases, however, the spleen went down in size very rapidly, so that, by about a fortnight from the commencement of treatment, a spleen previously enlarged to about 3 or 4 inches below costal margin became quite replaceable under the costal margin. Table VI shows the analysis of the size of the spleen of the patients before and after treatment.

Improvement in other clinical features and blood findings

There was progressive improvement in the general condition during the course of injections in all patients except those who had complications such as dysentery or pneumonia during the treatment. There was a variable degree of generalized oedema in some cases. The oedema began to subside within a few days of the commencement of treatment with M.&B. 800, and in every case it disappeared within a week of the completion of the injections. This led to some initial loss of weight in certain cases, but ultimately almost all these patients, as well as the others, gained in weight; this fact will be evident from table VII. Maintenance of

I
diamidino-di-phenoxy-pentane

11	12R	13	14R	15R	16	17	18	19	20R	21R	22	23R
Ind.	Ind.	Ind.	Ind.	Ind.	Ind.	Ind.	Ind.	Ind.	Ind.	Ind.	Ind.	Ind.
22	6	40	8	38	29	15	27	12	24	6	11	5
M.	M.	M.	F.	M.	M.	M.	M.	M.	M.	F.	M.	F.
5	36	110	42	104	100	64	87	39	88	24	47	18
8	15	7	8	2	7	8	1	3	2	9	(1)	24
6.18	7	6½	4	3½	3	3½	P.	2	7	4½	5	5
1.1	3.43	9.21	6.05	8.25	3.98	7.012	9.625	5.5	6.18	6.73	6.87	6.18
+	1.8	5.0	1.6	1.5	1.3	1.7	3.3	1.6	2.0	4.0	2.8	7.6
+	+	+	+	+	+	+	+	+	+	..	+	+
0.075	0.375	1.11	0.495	1.13	0.820	0.565	0.745	0.45	0.960 0.960	0.275	0.400	0.225
..	1.041	1.009	1.178	1.086	0.820	0.882	0.856	1.153	1.09 1.09	1.145	0.851	1.25
2	12	12	12	12	10	10	10	12	12 12	12	10	12
..	10.4	11.0	11.0	11.41	8.8	10.1	11.0	11.275	..	11.5	12.375	11.55
..	3.9	5.5	6.3	4.3	6.2	5.7	5.6	8.1	..	12.0	8.4	7.4
..	2½	3	2½	P.	O.	O.	P.	O.	..	O.	R.	R.
D.	36*	115	52	119	112	66	87	54	C.	28	51	24½
	C.	C.	C.	C.	C.	C.	C.	C.	C.	C.	C.	C.

* (Edema on admission, nil at the time of discharge.

PROTOCOL II

Further details regarding the resistant cases

Case number	PREVIOUS TREATMENT			DIAMIDINO-DI-PHENOXY-PENTANE	
	Drug given	Amount	Result	Total dosage	Result
6	Urea stibamine	1.15 gm.	Little effect on fever	0.305 gm.	Died.
10	? Pentavalent antimonial	24 injections	Little effect	0.960 gm.	Cured.
12	Urea stibamine	1.6 gm.	Little improvement	0.375 gm.	Cured.
14	Urea stibamine	1.525 gm.	Little improvement	0.495 gm.	Cured.
15	Urea stibamine	2.2 gm.	Cure followed by relapse	1.130 gm.	Cured.
20	Diamidino-stilbene	0.635 gm.	Cure followed by relapse	1.920 gm.	Cured.
21	? Pentavalent antimonial	24 injections	Little effect, developed cancer oris.	0.275 gm.	Cured.
23	Neostibosan	6 injections	Little improvement	0.225 gm.	Cured.
	Neostibene	1 injection			
29	Neostibene	0.165 gm.	Improvement followed by relapse.	0.775 gm.	Cured.
	Solustibosan	11 injections			
	Diamidino-stilbene	0.305 gm.	Apparent cure followed by relapse.	1.040 gm.	Cured.
31	Diamidino-stilbene	0.635 gm.			
32	Urea stibamine	22 injections	Little improvement	0.865 gm.	Cured.
	Neostibosan	12 injections			
	Neostibene	10 injections			

weight at the same level in one case and loss in another was apparently due to loss of extensive oedema, after treatment.

From table I it will be seen that before treatment the mean hæmoglobin per cent was 6.591 ± 1.549 g. per 100 c.cm. of blood and that the figures were 10.573 ± 1.38 g. after treatment. These figures indicate a marked general improvement in the hæmoglobin level.

The figures relating to the total leucocyte counts are given in table II. The mean and standard deviation of the leucocyte counts was 2.718 ± 1.52 thousand per c.mm. before treatment and 6.43 ± 2.35 thousand per c.mm. after

treatment. Here also a marked increase in the leucocyte count after treatment is evident.

Failures.—In one case only, the drug was entirely unsuccessful, though two full courses of injections were given. Further details of the case are given below:—

Case 24.—Indian male, aged 26 years, was admitted for intermittent fever for 3 months, slight cough with expectoration about 1 month. The liver was enlarged $\frac{1}{2}$ inch and the spleen $3\frac{1}{2}$ inches below the costal margin. The heart and lungs showed no abnormality. Leishmanize were found on spleen puncture and the patient was put on a course of M.&B. 800. He had 10 injections from 6th October to 15th October, 1942 (total dose 0.740 gm.). The temperature came down to some

extent, but persisted at about 100°F. He was given a course of aleerin (an atebrin-like compound) for giardial infection and a possible latent malarial infection. Though the giardial infection was eradicated, the low pyrexia continued. About the middle of November 1942, the temperature rose to higher levels and gradually became remittent in type. He was then given the second course of injections of M.&B. 800 (10 injections, total dose 0.740 gm.). The temperature came down to some extent. The fever was intermittent in type, rose to about 100°F., and was unaffected by cinchona. The patient was subsequently treated with neostibosan (15 injections, total dose 4.4 g.) and the temperature was normal from the day of the 11th injection.

TABLE VI

Size of the spleen before and after treatment

Degree of enlargement. Inches below costal margin	Number of cases before treatment	Number of cases after treatment
0	0	6
Up to 1	3	12
< 1-2	3	1
< 2-3	2	6
< 3-4	5	2
< 4-5	6	0
< 5-6	1	0
< 6-7	7	0
TOTAL	27	27

TABLE VII

Weight	Number of cases
Increase by 7 lb. or less	15
between 7 lb. and 14 lb.	5
14 lb. and 21 lb.	3
Weight remained the same	2
" reduced	2

Deaths.—Two patients, one a 'resistant' case and one an 'ordinary' case, died. Further details of these cases are given below:—

Case 6.—The patient came from Assam, where he had been suffering from kala-azar for one year. Before admission he had twice-weekly injections of ureastibamine, total dose 1.15 g., without any improvement. He had 9 injections of M.&B. 800 in the hospital—total dose 0.305 g. During the course of treatment for kala-azar, he developed acute otitis media and was receiving treatment for this condition also. On the day of his death, the patient suddenly started violent convulsions about noon. The usual treatment, including inhalation of chloroform, was tried without any effect, and he died. Two days prior to his death the discharge of pus from the ear had diminished markedly.

Case 2.—The patient was admitted on 24th September, 1942, for irregular attacks of fever and progressive weakness—duration 5 months. On admission he was found to be gravely ill. He was markedly anæmic and there was slight icteric tinge of the conjunctiva. He had a high remittent fever—the temperature varying about 103°F., the pulse rate was 140 per minute and the respiration 30 per minute. There were signs of bronchitis over both lungs. The spleen was enlarged up to 8 inches and the liver 2½ inches below the costal margin.

The patient was put on stimulants and expectorant mixture. Leishmaniae were demonstrated in the sternal puncture smear and he was put on injections of M.&B. 800 on 26th September. The first dose was 0.025 gm. and the second on 27th September, 0.050 gm. On 28th September, the patient was very much worse, and was found to have tarry stools and a few purpuric patches. The urine now showed the presence of albumin and granular casts, pus cells, and leucocytes in fair number. The hæmorrhage was persisting in spite of all hæmostatic measures, and the patient had severe pain in the abdomen. The blood showed severe thrombocytopenia, and increased coagulation and bleeding time. (For blood report see table.) On 1st October, he was given a transfusion of citrated blood (100 c.c.m.)* but these measures did not have any effect and the bleeding continued. Large patches and ecchymoses appeared and the melæna continued. The patient died on 2nd October, 1942.

Blood counts

	25th September, 1942	28th September, 1942
Hæmoglobin ..	6.187	6.187
Red blood cells ..	2.78	2.70
Cell volume ..	21.4	22.6
MCV ..	77.0	83.7
MCH ..	22.2	22.9
MCHC ..	28.9	27.3
Leucocytes ..	1,110	1,500
Neutrophils % ..	56	..
Lymphocytes % ..	33	..
Monocytes % ..	11	..
Eosinophils % ..	0	..
Basophils % ..	0	..
van den Bergh test	0.8 mg.	Direct delayed + 1.25 mg.
ESR ..	56	..

Discussion.—From the above paragraphs giving a detailed analysis of the results of treatment, it will be evident that diamidino-de-phenoxy-pentane has well-marked anti-kala-azar activity. Of the twenty-one ordinary patients, nineteen made an immediate recovery and one died. This fatal case can hardly be regarded as one belonging to the series of cases treated with this drug, because he had only two very small doses of the drug and was gravely ill at the time of admission. If we omit this case, of 20 cases 19 recovered, and in one case this drug was unsuccessful. Of the 19 cases that recovered, one subsequently relapsed. But it is well known that with any form of treatment, a small proportion of cases will relapse and require a subsequent course of treatment.

The 'resistant' cases responded quite satisfactorily to this drug. Of eleven cases all except one (fatal case) were apparently cured. This patient died of associated complications.

The question of complete cure.—From the all-round improvement, i.e. absence of fever, increase of hæmoglobin and leucocyte counts,

* The transfusion was limited to 100 c.c.m. only as the patient had a dilated heart, and the transfusion was given only to supply platelets to the thrombocytopenic patient.

decrease in size of the spleen, gain in weight, of the cases that showed immediate cure, it is probable that most of them made a complete recovery. But the clinical criteria of cure, as well as the protozoological, are very misleading, and some of the cases showing few of the features of improvement mentioned above may be cured, while other cases showing almost all of them may relapse; the senior writer discussed the question of criteria of cure on various occasions (Napier, 1926-32, Napier *et al.*, 1937, Napier, Sen Gupta and Sen, *loc. cit.*). He is of opinion that there is no certain immediate criterion of cure, and that time alone can indicate if an apparent cure is a complete cure. It may be said that if a patient relapses, he does so within 6 months after a course of treatment. In this preliminary report, we are not able to present a follow-up report of the cases, as in most of these treatment finished less than four months ago.

With regard to immediate reactions to the intravenous injection of diamidino-di-phenoxy-pentane, we have found that these reactions are much less severe than those with diamidino-stilbene, and in no case was any serious or even alarming reaction caused by this drug.

Summary

Thirty-two cases of Indian kala-azar, 11 of which were 'resistant' cases, were treated with diamidino-di-phenoxy-pentane. Ten out of the 11 'resistant' cases and 19 out of the remaining 21 ordinary cases were apparently cured. In one case the drug was unsuccessful in effecting a cure, and in one 'resistant' and one 'ordinary' case the patient died of associated complications. Intravenous administration of this compound was not attended with any serious or alarming reaction.

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RECURRING PELLAGRA SYNDROME IN A MYXŒDEMATOUS SUBJECT

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WE do not propose to discuss here the various theories regarding the ætiology of pellagra. However, it is now definitely established that pellagra is intimately associated with the vitamin-B₂-complex fraction, niacin (nicotinic acid), usually being due to its deficiency in the diet but also to its mal-absorption from the gut.

Thus, pellagra is normally a disease of poor populations, whose food is poor in vitamins and protein, or of institutions where the diet charts have not been designed wisely, or where, for some other reason, suitable food cannot be, or is not, supplied.

Sporadic cases are encountered from time to time in 'normal' mixed populations, and the patients are not by any means always the poorest members of such populations. This has been our experience in Calcutta, but, from the majority of such cases, we have been able to elicit a history that suggested a period of restricted dietary, or of some other determining factor such as alcoholism.

Pellagroid symptoms occur sometimes in sprue and other similar condition on account of the failure of absorption of niacin.

The case that we are reporting is of special interest in that there is no evidence either of dietary deficiency or of any bowel condition that might be associated with mal-absorption. Further, despite successful treatment, the condition persistently relapsed.

The condition was not cured by giving a well-balanced diet, but required niacin in maximal doses; the striking thing was however that cure could be equally well effected by the administration of thyroid extract in doses up to 10 grains daily.

This patient has been under our observation for a period of over five years, during which time he has been admitted to hospital on four occasions. He has also incidentally provided valuable clinical material for five consecutive D. T. M. classes. His clinical history is given briefly below, and some of the observations made are shown in the tables.

A Hindu male, aged 45 years, a widower, was admitted into the Carmichael Hospital for Tropical Diseases for the fourth time on 15th December, 1942, for relapsing pellagra. The three previous admissions to the hospital had been during the month of January 1939, 1941 and 1942, and on each occasion the diagnosis of pellagra was made.

He has no occupation; he is a property owner. His diet is fairly liberal; he takes three meals a day, which include fish, egg, fruits and milk

almost regularly and meat periodically. He does not take alcohol; he smokes and chews tobacco, with *pan* at times.

There is nothing particular in the family history. His parents died in old age. He has a son and a daughter, both healthy.

The past health of the patient was not very good. He suffered from dysentery, 'sunstroke', small-pox, and typhoid at the age of 1½, 4, 6 and 12 years, respectively. He has had a chronic discharge from the left ear since childhood. In 1923, he suffered from a severe attack of flatulent dyspepsia. Medicine failed to relieve him, so he went for a change of air, and improved after six months. Next year, the trouble started again—he was constipated, bowels opened twice in a week—and, as a result of straining at stool, he developed piles that used to bleed at times. With medical treatment and repeated change of climate, he recovered his health again, but his 'dyspepsia' and piles troubled him now and then.

In 1937, all his symptoms were aggravated. Besides flatulence and constipation he had indefinite pain in the abdomen. He lost his appetite completely. The piles bled profusely;

he became anæmic; and the hands and feet were swollen. Subsequently, about the month of October, he noticed for the first time a roughening and darkening of the skin of the outer aspects of the arms and forearms, and on the instep. He consulted our skin clinic in the month of December, when apparently a diagnosis of scleroderma was made, and he was put on to thyroid extract. The skin condition had gradually cleared up by March 1938.

Thereafter, every winter he developed pellagrous eruptions. Usually his symptoms began about the month of October each year (with the arrival of goddess Doorga, as he says). They generally included dyspepsia, flatulence, abdominal discomfort or pain, alternate constipation and diarrhoea or dysentery, anorexia and cramps, occasional sore tongue (usually during a diarrhoeal attack), insomnia, giddiness, and forgetfulness. He felt cold and therefore exposed himself to the sun more than usual and got sunburnt. The dorsum of the hands was discoloured first and then various other parts. The condition usually became worse at Christmas time each year, and he sought admission to our hospital. In 1940, he could not come to us owing

A summary of the case notes during his various stays in hospital are given in table

Summary of clinical notes	January 1939	January 1941	January 1942	December 1942
Pellagra dermatitis	+	+	+	+
Flatulent dyspepsia	+	+	+	+
Pain abdomen	Not noted	+	+	+
General weakness	+	Not noted	+	+
Puffy face	Not noted	+	+	+
Œdema legs	+	Not noted	Not noted	+
Thickened sigmoid colon	Not noted	+	+	—
Tongue	Coated	Coated	Coated	Coated
Double hydrocele	+	+	+	+
Microfilaria in blood	+	+	+	+
Thick voice	+	+	+	+
Bleeding piles	Not noted	+	+	+
Weight (lb.)—				
On admission	135½	116½	125½	122
On discharge	142	120½	142	110/70
Blood pressure	100/80	95/65	Not noted	
Mental state	—	—	—	Dull and depressed.
Gastric analysis	Achlorhydria (histamine not tried).	Hypochlorhydria (almost achlorhydria).	Histamine-fast achlorhydria.	Histamine-fast achlorhydria.
B.M.R.	—	— 53%	— 41%, on discharge — 19%	— 27%
Blood count				
Date	21-1-39	21-4-41	9-1-42	16-12-42
Hæmoglobin	102% = 14.02 gm.	88% = 12.1 gm.	84% = 11.5 gm.	84% = 4.5 gm.
Reticulocyte	0.5%	0.6%	0.2%	0.2%
Red cells per c.mm.	4.31	4.35	4.33	4.40
Cell volume %	38.5	38	33	36
MCV	89.5	95	76.2	81.8
MCH	32.6	30.2	26.7	26.2
MCHC %	36.8	31.8	35	32
White cells per c.cm.	7.5	8.7	6.6	7.6
Neutrophils %	55	79	63	62
Lymphocytes %	32	16	25	31.5
Large mononuclears %	4	4.5	6	4.5
Eosinophils %	9	0.5	5	2
ESR (1 hour, Westergren)	—	—	—	30 mm.
Wassermann reaction negative.				

to his father's death; he had private treatment which included injections of campolon and vitamin B₁.

During the months from April to August or September, he generally kept well. In order to prevent further relapse, he was careful about his diet, and took marmite, nicotinic acid and/or thyroid at intervals during this period for the last two years.

Treatment.—1939. Acid pepsin mixture.

1941.—Thyroid gr. $\frac{1}{2}$ b.d. for 15 days. (General appearance improved, otherwise no change.) Then put on nicotinic acid 500 mg. daily for 10 days (patches began to clear in 4 days) and 250 mg. daily for 20 days.

Thyroid (in addition) started on the 17th day of nicotinic acid treatment. Dose up to 3 grains a day. (Skin lesions cleared up within 3 weeks of nicotinic acid therapy.)

January 1942.—The patient was put on nicosil, 5 tablets a day (each containing 0.5 mg. of sulphanimide and 20 mg. of nicotinic acid), with thyroid extract, gr. i, twice a day. No improvement was noticed after a week's treatment. Next, the thyroid was increased to 4 grains a day, and nicotinic acid was started in place of nicosil, in daily doses of 500 mg. for the first four days and then 100 mg. Desquamation started on the third day of nicotinic acid. The lesions gradually cleared up and there was marked improvement in the general condition.

Present attack.—Towards the end of September 1942, his dyspepsia returned; it was associated with anorexia, abdominal pain, flatulence and obstinate constipation with occasional bouts of diarrhoea. A rash appeared on the dorsum of hands in October when he first attended the School, but he refused admission into the hospital. He appeared disappointed that his condition had relapsed despite all possible precautions. Hence, this year, he decided first to try some amateur therapy, i.e. besmear the body with mud, sit in the sun, and then bathe in the Ganges. We pointed out to him the serious risk of sun trauma, and observed the experiment with interest. He came to see us periodically; the condition seemed worse each time he came, and finally, with a good deal of persuasion, he consented to be admitted into the hospital once more.

Examination.—The patient was fairly well-nourished. The face was pale and puffy with baggy eyelids; the appearance was that of typical myxœdema. There was thinning of the outer half of eyebrows, his temperature was 96.6°F., pulse 64, and respiration 16 per minute on admission.

Skin.—The skin was dry and rough, and there was little sweating. There was typical pellagrous dermatitis (plate VII, figures 1 to 3). Some of the patches, especially those on the dorsum of the feet and hands, had a dirty black colour; the epidermis was thickened and showed transverse fissures, some of them being deep and covered with a dry exudate. There were two

erythematous patches (like severe sunburn or first-degree burn) over the right calf without any corresponding ones on the left side. They had appeared recently and were painful and tender. The skin over the greater trochanter of each femur and over the coccyx was deeply pigmented. The perineal region was also darkened. Symmetrical dermatitis was also present in the upper extremities, involving the outer aspects of the hands, forearms, and lower part of the arms. It extended partly to the inner aspect of the forearms. The margin was sharply demarcated and more pigmented than elsewhere, with transverse fissures at irregular intervals, while the central part was desquamating, exposing smooth thin skin. Slight itching of the affected part was complained of, but there was no pain or tenderness. Dermatitis of a similar nature was present over both shoulder regions, and behind the neck. There was a tender erythematous patch of recent origin over the lower part of the right scapula with no corresponding lesion on the other side. The forehead was slightly pigmented.

Evolution of the dermatitis.—We noticed that it usually began as a patch of erythema resembling severe sunburn, associated with an uncomfortable or even painful tension. Later a deeper dermatitis developed with dirty black pigmentation and thickening of the dermis. Finally, atrophy supervened, the skin became wrinkled and thin, and then desquamation commenced in the centre of the patch. The sharp pigmented border cleared up last.

Gastro-intestinal symptoms.—The patient on admission had no appetite; most of his food remained in his locker untouched. Diarrhoea, with 4 or 5 stools daily, from which he had suffered for a week, continued. He also complained of excessive salivation, and pain in the abdomen, 'twisting' and at times griping in character. The tongue was thick and smooth; it was not sore or red. (He had noticed occasional sore tongue previously, especially during the bouts of diarrhoea.) The abdomen was soft, with deep tenderness over the cæcum and gall-bladder regions. The liver and spleen were not palpable.

Circulatory system.—The patient complained of occasional palpitation and precordial distress. The heart appeared to be of normal size, and the sounds were clear. There was a tendency to bradycardia. There was slight œdema of the ankles.

Nervous system.—The patient was weak, lethargic and slow in action. He was depressed and often expressed fear that he had now come to the last stages of his chronic illness. He complained of vague generalized pain and tightness in the body; he slept badly; the speech was slow and thick; his knee and ankle jerks were lost, but the supinator, biceps and triceps jerks, and superficial abdominal reflex were present; the pupils were equal and reacted to light and accommodation; his sight was normal; there was

a chronic discharge from the left ear; his hearing was unaffected; except for some slight impairment of sensation over the thickened skin, especially of the ankles, and some calf tenderness, there were no objective sensory disturbances; the muscle and joint sense and the sphincter control were normal, and there were no tremors.

Other features.—There was a tendency to sub-normal body temperature, and he felt bitterly cold all day. He had double hydrocele and enlarged glands in the groin, presumably of filarial origin.

Course in the hospital.—During the first few days after admission, he remained in a miserable state with severe dry dermatitis, diarrhoea with indefinite abdominal pains, and flatulence. He was completely apathetic about food, and remained mentally depressed. He was given a carminative mixture and encouraged to take nourishment while investigations were being carried out. The diarrhoea subsided spontaneously.

He was then put on thyroid in gradually increased doses. Apart from local applications of vaseline he had no other treatment. Ordinary hospital diet was given. His piles bled for a few days, for which a palliative treatment was prescribed.

Clinical improvement of the patient's condition was observed about 12 days after thyroid therapy was commenced. He felt better and took an interest in his surroundings; his appetite returned. There was definite progressive clearing of the skin lesions, and no more fresh patches appeared. The acute erythematous patches on the right calf and scapula did not progress further; the skin became wrinkled and peeled off.

The patient is still in the hospital, now having 10 grains of thyroid extract daily. There has been remarkable subjective and objective improvement. He is free from pain and dyspepsia; the skin lesions have undergone almost complete resolution (plate VII, figure 4). His present weight is 117½ lb.; blood pressure 115/72 mm. of mercury, pulse 80 and respirations 20 per minute.

Summary and conclusion

This is a typical case of pellagra; the interesting features are that the condition persistently relapsed every winter for five years; that there is associated myxœdema; that there is no clear evidence of dietary deficiency or of any abnormal bowel condition that might be associated with mal-absorption; and that the condition was not cured by giving a well-balanced diet, but there was prompt response to niacin or thyroid extract in maximal doses. The patient tolerated 10 grains of thyroid extract daily. The dermatitis, usually most marked in the winter, was aggravated because at this time he exposed himself to the sun. The state of hypothyroidism aggravated his intolerance of cold. The inner aspect of the calves is an unusual site for a

(Concluded at foot of next column)

DEVELOPMENTAL ANOMALY OF SEX-ORGANS

A CASE NOTE

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THE developmental anomaly of the simultaneous possession of male and female genital parts is known as hermaphroditism. This condition is known to occur in different degrees. True hermaphroditism, i.e. the occurrence of both ovary and testis, is however rare (Feldman, 1937). Recently we have come across a case of an apparently male person having both testis and uterus. Considering the rare and interesting points exhibited in this case, we are reporting it.

Before we describe the case we outline certain facts from the developmental point of view which will enable the case to be easily followed.

In the vertebrates, the development of the urinary and genital systems takes place from a common genito-urinary ridge. They arise from the intermediate cell mass, a part of the mesoderm. From this the nephric tubules and the genital glands are developed.

In the lower vertebrates, the excretory or nephric tubules serve for the conveyance of both urine and the cells of reproduction, as can be seen in the male frog. In the frog if we examine the intermediate cell mass, we find that it is channelled by a canal connecting the coelomic cavity with the myoele. From the dorsal aspect of this channel, nephric tubules develop and from the ventral wall, the glomeruli are formed and protrude into this part of the cavity.

In humans, the excretory system is based on this common system with certain modifications. The hollow somatic stalk (i.e. the coelomic cavity portion in the intermediate cell mass) in the lower vertebrates is however not found in the higher vertebrates including man, but the solid mass contains all the potentialities of all the somatic stalks. Glomeruli and tubules, with the cavities around the glomeruli, are formed in it.

(Continued from previous column)

pellagrous lesion, but in this case it was obviously due to the sun trauma caused by sitting in the sun in a squatting position with the legs exposed. The patient has chronic achlorhydric gastritis, a common finding in pellagra, but this is also encountered in 4 per cent of normal individuals.

This case seems to demonstrate very clearly a reciprocal action between the endocrines and the vitamins.

Although further observation of this case is desirable, there appears to be strong evidence that cure of the symptoms of pellagra can be effected either by niacin or by thyroid extract.

PLATE VII

RECURRING PELLAGRA SYNDROME IN A MYXEDEMATOUS SUBJECT : L. E. NAPIER AND
R. N. CHAUDHURI. (PAGE 183.)



Fig. 1.—Before treatment.

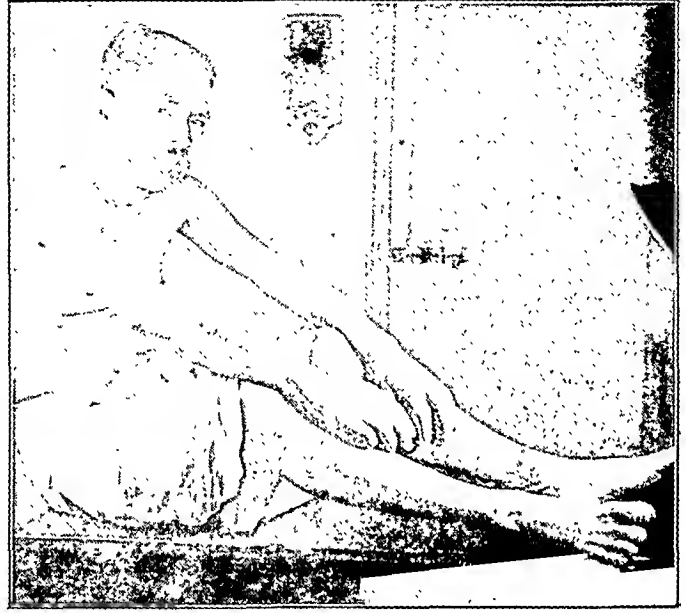


Fig. 2.—Before treatment.



Fig. 3.—Before treatment.

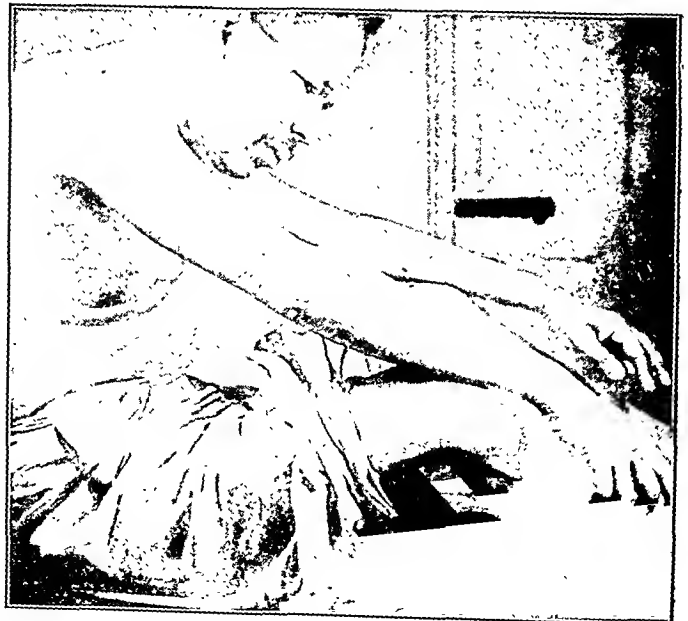


Fig. 4.—After treatment.

PLATE VIII

DEVELOPMENTAL ANOMALY OF SEX-ORGANS : MACPHERSON, TRIBEDI AND BANERJEE

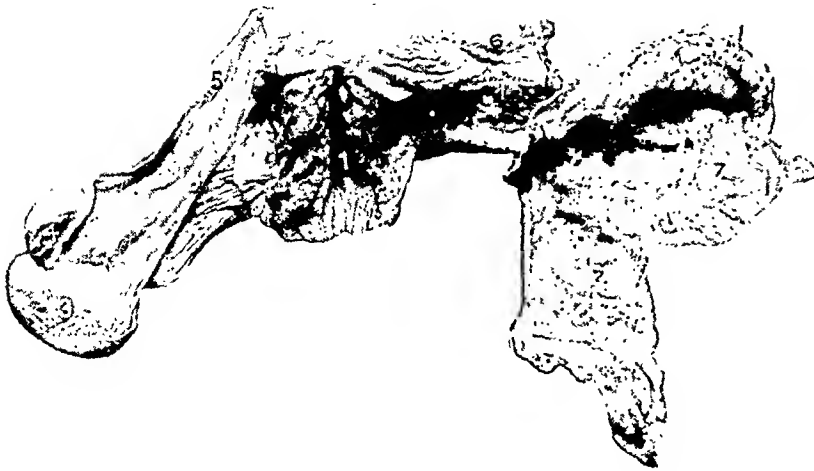


Fig. 3.—(1) The uterus. (2) The right peritoneal fold. (3) The oval body. (4) The pea-shaped mass. (5) and (6) The fibromuscular tubes at the upper ends of the right and left peritoneal folds. (7) A part of the hernial sac. (8) The ridge produced by the tubes within the right peritoneal fold.



Fig. 4.—Section from the uterus showing the endometrium and the fibromuscular tissue.

AN UNUSUAL FRACTURE : M. S. MAHMOOD. (PAGE 200.)



In the evolution of the higher vertebrates, a succession of three renal systems is found, the third being the present functional kidney. These are the pronephros, the mesonephros, the Wolffian body, and the metanephros. In the embryo of the sixth week, all three systems may be seen. About this time, it can be seen that the pronephric system, which is developed in the last four or five cervical and first two or three thoracic segments, is undergoing regression, that the metanephric system in the hinder lumbar segments is only just appearing, and that the Wolffian body is approaching the height of its development. In the third month, the permanent kidney assumes its predominant position, and its predecessor, the Wolffian body, is converted into a mere appendage of the genital system.

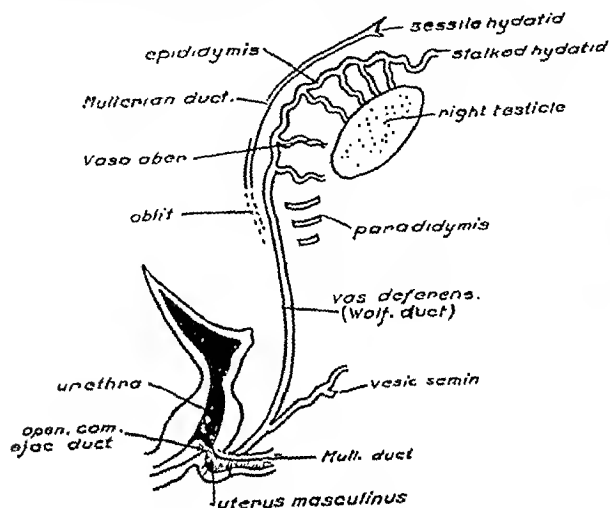


Fig. 1.—Remnants of the Wolffian body in the male. (After Keith.)

Though originally extending from the fifth cervical to the third lumbar segment, by the eighth week the Wolffian bodies are confined to the region of the lower three thoracic and upper three lumbar vertebrae, where they project into the abdominal cavity on each side of the dorsal attachment of the mesentery. To its inner side in the lower dorsal region lies the genital ridge. The growth begins during the fourth week as a thick mass, later being separated from the Wolffian body by having its own mesentery. The genital and the Wolffian bodies have thus each their own mesentery; but these two mesenteries have a common attachment (common uro-genital mesentery).

At first the hinder or pelvic ends of the Wolffian bodies are separate, but in the eighth week they become approximated in the pelvic region, and fuse to form the genital cord. The genital cord contains the terminal parts of the Wolffian and Mullerian ducts.

After the sixth week, the Wolffian body undergoes degeneration. In the upper part, some tubules (6-12) are left, which later form a part of the duct system of the testis, and lose their connection with the glomeruli and secreting tubules, which disappear. The caudal portion of the body continues to degenerate, finally remaining as a remnant of a few atrophic tubules which have lost their glomeruli and their connection with the duct. Structures derived from the Wolffian duct in adult human beings are shown in figures 1 and 2.

In addition to these, the ureter and collecting tubules of the kidney are also developed from the Wolffian body. The Mullerian ducts are formed from the *ostia abdominale* (peritoneal funnels) which appear on the ventro-lateral aspect of the Wolffian ridge as funnel-like invaginations of the coelomic mesothelium. From this, a solid rod-like process of cells grows backwards on the Wolffian ridge ventral to the Wolffian duct, reaching the region of the cloaca in the eighth week, and passing below and internal to the Wolffian duct.

The right and left ducts fuse in the genital cord almost at once, where they give rise to the development of uterus and vagina. In the male embryo, the Mullerian ducts are also completely and strongly formed, and give rise to the sinus pularis or uterus masculinus in the prostate.

Descent of the genital glands. Part of the Wolffian ridge is continued backwards as a peritoneal fold to the groin, forming the inguinal fold. Within this fold, as well as in the mesentery of the Wolffian body and the gonad, and also in the genital ridge, is a tissue

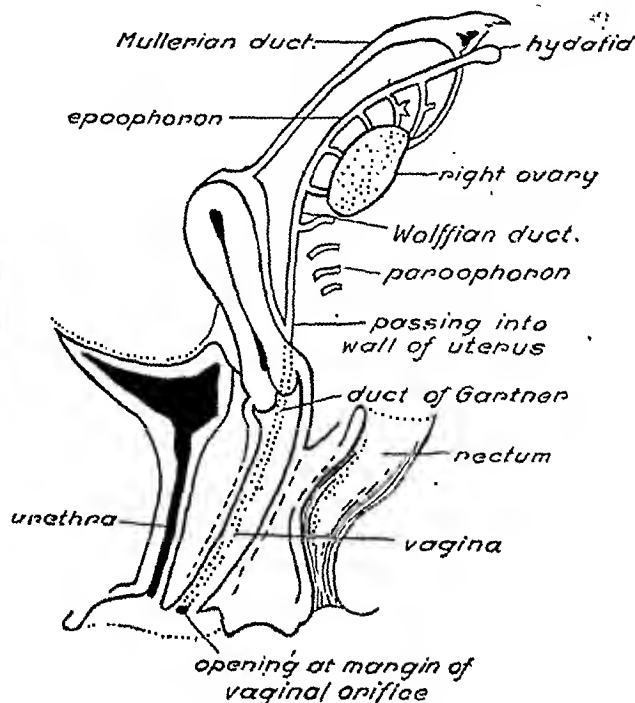


Fig. 2.—Remnants of the Wolffian body in the female. (After Keith.)

rich in non-striated muscle derived from the sub-peritoneal connective tissue. It is endowed with plastic properties. In the third month the mesodermal tissue in the lower end of the fold begins to pierce the abdominal wall external to the deep epigastric artery. The growing end carries in front all the walls of the abdomen plus the peritoneum, and comes to rest either in the scrotum or the labium majus. The lower pole of the testis at this time can be seen to be close to the abdominal wall, i.e. the inner ring, through which the gubernaculum passes. Towards the end of the seventh month, the gland passes through the inguinal canal and in the eighth month it is in the upper part of the scrotum. This is what is termed the descent of the testis.

Case note

A mass was removed by operation from a man aged about 45 to 50 years, who was suffering from a large (right) inguinal hernia. The scrotum was empty; there were no testes; the patient said that 'two testes' came down on the right, appearing and disappearing. The penis was normal and he said...

Operation.—On opening the hernial sac, the whole mass was seen inside it. One 'testis' was seen at the internal abdominal ring; next was found the lump after which the other 'testis' was found. The whole mass was removed, leaving one testis which seemed to have an

epididymis and a tubular structure; this was put into the scrotum.

Description of the specimen (plate VIII, figure 3)

In the centre there was a structure which appeared to be a uterus. It measured 6.5 cm. in length. The fundus and the cornua were not well developed. No opening leading to the fallopian tubes could be seen. The uterine body was not very well differentiated from the cervix, the organ having a more or less tubular structure. The endometrial lining was very thin but recognizable. The wall seemed to be very fibrous. The peritoneal covering at the top was intimately connected with the uterus and could not be separated without injuring the wall of the uterus. The uterus ended abruptly at the cervix. No vaginal portion was found. On the right side of the uterus, at the extreme end of the peritoneal fold, was an oval body which, on section, presented a pale amber colour. This oval structure measured 4 cm. by 2.5 cm. About 2.5 cm. above this was seen a pea-shaped body. It showed a coarser structure having a yellow colour. Leading away from the upper pole of the pea-shaped body was a thickened ridge of peritoneum extending up to the upper part of the uterus. On dissection, the mass was found to consist essentially of fibromuscular tissue intimately adherent to the peritoneal coat, but no distinct cavity could be seen. In between the folds of the peritoneum were seen several small tubes arising with a broad base from the attached border of the oval body and going towards the uterus. These tubes constituted a distinct swelling on the posterior aspect of the fold of the peritoneum, which was specially noticeable on the posterior part as an oval mass by the side of the uterus. These fine tubular structures were seen to be connected with the pea-shaped body. These extended towards the uterus in three musculo-fibrous strands, one along the free border of the peritoneum and the remainder through the centre of the fold, all of them ending in an oval mass by the side of the uterus. The latter was found to send several fine tubular twigs to the surface of the uterus, where a large tortuous tube was seen to descend to the lower part of the cervix. On the left side of the uterus, in the peritoneal fold at its free upper edge, was seen a fibromuscular tube with a lumen. In the middle part of the same fold there was a thick fibromuscular strand ending in an oval mass similar to that on the right. The left of this was a portion of the wall of the sac in which the uterine mass was enclosed.

Microscopical examination

The tubular organ in the centre showed the structure of a uterus; the muscular element was not very well developed. The endometrium was thin and lined with a layer of columnar epithelium with a few simple glands. The stroma was scanty and not well developed, but the structure was distinct and recognizable (plate VIII, figure 4). The oval body showed the structure of testicular tissue which is usually found in an ectopic testis. The tubules were fairly numerous, though slightly more separated from each other than is usual. The wall of the tubules showed marked hyalinization. In many places the cavities of the tubules were almost obliterated by foamy, polyhedral, epithelial cells resembling the cells of Sertoli found in the ectopic testis. No spermatogonia were found. In between the tubules, the fibrous tissue was seen to be increased, and showed hyperplastic Leydig cells (interstitial cells of the testis) within it. At one corner could be seen a few tubules lined by low cubical epithelium somewhat resembling the rete-testis. No ovarian structure was seen in any part of the testis. The tubes on the left side showed a fibromuscular tubular structure with a well-developed lumen lined by one to two layers of cubical cells. The pea-shaped mass at the top of the testis showed a collection of tubules with well-defined acinar spaces and lined by a layer of low columnar epithelium. Its structure resembled somewhat that of

the epididymis. The fine tubules leading away from the testis in a wedge-shaped manner showed a mass of tubes having fibromuscular walls and a lumen incompletely and scantily lined with a layer of flattened epithelium. Histological sections from the different cords showed the structure similar to the above. Along with them were blood vessels.

Sections from the masses on the right and left of the uterus showed the cross sections of tubes lined with a well defined columnar epithelium. At some places it had formed papillary projections. The section of the fibromuscular band leading away from the right side of the uterus, showed the same structure as on the left, viz., a fibromuscular tube, the lumen of which was lined by a single and in some places double layers of low cubical epithelium. No papillary projection inside the lumen could be seen.

Discussion

A true hermaphrodite is a person in whom gonads of both the sexes are present, but when the external genitalia are of one sex and the internal gonads are of the other, the term pseudo-hermaphrodite is used. The appearance of the external genitalia is really due to incomplete and faulty development. Thus a person with a gonad of a male and with a female type of external genitalia is a male pseudo-hermaphrodite, and an individual with a gonad of a female and with male type of external genitalia (probably due to fusion of labia and protrusion of clitoris dragging the urethra under it) is a female pseudo-hermaphrodite. Now in this present case several interesting questions arise. (1) What is the sex status of the patient? (2) How can the developmental anomaly be explained? (3) What is the explanation of the unilateral presence of 'testis' and 'uterus'? (4) How can we explain the man's having children in view of the non-fertilizing power of the ectopic testis?

Firstly, apart from the uterus and the two tubular structures intimately connected with the uterine body, the identity of which is not very clear, no female characteristics have been detected. In the absence of any histological study of the other 'testis', which seemed to have an epididymis and a tube, we do not know, from the clinical material available at our disposal, what was the real nature of the above structures. If it is an ovary and a fallopian tube, then of course the presence of a structure resembling the epididymis will be difficult to explain unless it could be some remnants of the Wolffian ducts and tubules. If this is so, then we can explain the presence of the uterus and two 'testes' on the same side, one being the testis and the other one an ovary. The tube-like structures in the right peritoneal fold arising from the testis and passing towards the uterus are the epididymis, ductus deferens and seminal vesicles, developing from the Wolffian duct and ending as Gartner's duct. In the male we find the ejaculatory ducts opening at the two sides of the uterus masculinus of the prostate which represents the uterus and the vagina. The second 'testis', we can presume, was probably also ectopic and was present in the other side of the abdomen. The presence of

the uterus, testes, and ovary if any, in the right inguinal canal could be explained by the abnormal drag by the specialized portion of the fibromuscular element on that part of the sub-peritoneal connective tissue represented by the gubernaculum testis and the round ligament of the uterus. From the study of the developmental features of the genito-urinary organs, we find that when the permanent kidney is developing (in the third month when the descent of the testis starts) the testis is lying in the so-called false pelvis, and the fallopian tube is crossing the Wolffian duct. If we consider that, in the descent of the testis, the Mullerian duct system has also been dragged into the right inguinal canal, then we can explain the presence of the uterus, ovary and testis on the right side and also the peculiar tubular shape of the uterus. Again, it is usually found that when the testis and the ovary develop from the same genital ridge, they are usually combined and not separate; thus the separation of these two structures will be difficult to explain. Microscopical examination of the testis at hand again is against the view that development of the ovo-testis is present only on one side. Also it is difficult to see how a unilateral drag could displace a uterus with its two tubes and an ovary and a testis (right) into the right hernial sac, leaving the other testis on the other side. Again, if we consider the structure in the left peritoneal fold to be the seminal vesicle because of the similarity of the microscopical appearance of the same structure in the right peritoneal fold, then we shall be at a loss to explain its presence as well as its persistence. This we can do if we assume that the other 'testis' is really a testis and the so-called epididymis and the tube is a real epididymis and the part of the Wolffian duct responsible for the development of the ductus deferens. If however we consider the other 'testis' to be the real testis, then how can we explain the presence of a uterus? Keith (1933) after Primrose (figure 5) has shown that the

and the cords along with the uterus and the tubes have been drawn into the right side.

So we are left to guess the true nature of the sexual status of the patient. Should we call him a pseudo-hermaphrodite or a true hermaphrodite? True hermaphroditism is embryologically possible because the early embryo possesses the rudiments of both sexes, namely the Wolffian ducts which develop into male organs other than the testes, and the Mullerian ducts, which are the precursors of the female organs other than the ovaries. Both the testes and ovaries probably develop from the genital gland, the former from the central or medullary portion, the latter from superficial or cortical portion. Hermaphroditism, therefore, is a condition in which there is a failure of one of the pairs of ducts to atrophy completely. This was so in Rutherford's case (1930), a normal boy with male external genitals and a uterus, tubes, and ovo-testes, found during an operation for inguinal hernia. In our present case we did not find the ovo-testis to explain the persistence of the Mullerian duct system. It may be considered that in sex differentiation there is an early development of the male sex gonads in the male to combat the influence of the female sex hormones in the placental circulation from the mother. In the female, the sex gonads develop late, since proper hormonal stimulus for the development of the female gonads is already coming from the mother. In the case under discussion, it is probable that the influence of the mother's hormonal stimulus was prolonged, while the hormonal influence of the male sex gonad was retarded. If this was so, then we can imagine the possibility of the development of the Mullerian duct system without the presence of the female gonads. If we take into consideration the findings recorded in the literature and the histological evidence of the testis of this case, it is difficult to understand the procreative power claimed by the individual in question. However it is not possible to be dogmatic unless we have studied the structure of the other 'testis'.

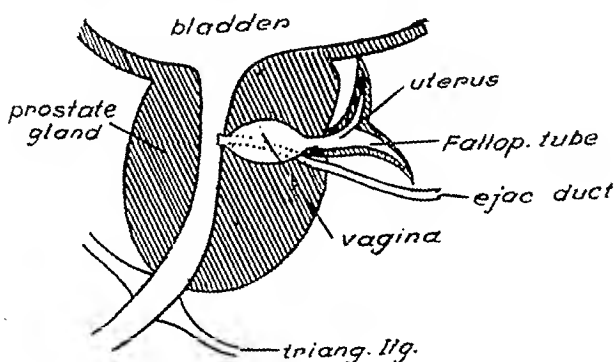


Fig. 5.—A section of a prostate showing the unusually developed uterus masculinus. (From Keith after Primrose.)

Mullerian element of the prostate may undergo development into a uterus with the fallopian tubes. It is not known how this development takes place. Probably by abnormal drag of the retroperitoneal fibromuscular bands, two testes

Summary and conclusion

1. A rare case of developmental abnormality of the internal sex organs is described.
2. The developmental aspect of the subject is discussed.
3. The sexual status of the individual is discussed.

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A STUDY OF INVASIVENESS AND TOXICITY OF CHOLERA, PARA-CHOLERA AND SAPROPHYTIC VIBRIOS IN ANIMALS

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(From the Cholera Bacteriological Inquiry, Indian Research Fund Association)

Koch (1886) studied the effect of cholera vibrios on guinea-pigs by feeding the animals with big doses of the organisms and then paralyzing the gut by intraperitoneal injection of 1 c.cm. of tincture of opium so as to delay evacuation. Out of 35 animals, 30 died showing weakness of the hind limbs and collapse. The small intestine was deeply injected and filled with a flocculent colourless fluid which contained *V. cholerae* in almost pure culture.

Thomas (1893) injected living vibrios intravenously into adult rabbits, and found ecchymoses and rice-watery fluid in the small intestine, containing large numbers of vibrios in the majority of the animals injected.

Experiments on rabbits were also done by several later workers.

Greig (1917) studied the effect of cholera and para-cholera vibrios on rabbits and pigeons, and found that the virulence of the vibrios showed considerable variation and that the M.L.D. of *V. cholerae* by intravenous injection into rabbits was somewhat higher than that of para-cholera vibrios.

Mackie (1922) injected separately cholera and para-cholera vibrios intravenously into rabbits and produced diarrhoea, rice-watery stools and subsequently death.

We tried in the following experiments to find out whether cholera, para-cholera and saprophytic vibrios can be distinguished by experiments on animals. Such a study has not been undertaken before.

Study of invasiveness

Enormous doses (10 millions to 20,000 millions) of live cholera vibrios given subcutaneously to a healthy man did not produce septicæmia, although there was marked local inflammation associated with pyrexia; but even small doses injected subcutaneously into guinea-pigs produced septicæmia in a half to two hours, and vibrios were finally excreted into the small gut. Young agar cultures of vibrios were suspended in nutrient broth and the opacity of the suspension was matched with a no. 1 Brown's opacity tube. (In earlier experiments no. 5 and no. 2 tubes were used for matching, but as the dose was found to be too high, in later experiments, only no. 1 was used.) Guinea-pigs are so sensitive to vibrios that enormous doses should not be used. One c.cm. of such a suspension was

injected subcutaneously into guinea-pigs of approximately 300 gm. in weight, and, 2, 18 and 36 hours after the injection, a large drop of blood was collected by means of a sterile capillary pipette, by puncturing the skin of the ear, and inoculated into alkaline peptone water. (In earlier experiments, blood was collected at intervals of half an hour, but later, the first specimen was taken 2 hours after the injection since it was seen that vibrios were as a rule found in the blood at 2 hours if they were already found after half an hour.) As the animals varied largely in their response, 4 animals were taken for testing each organism. Post-mortem examination was done on all the animals that died. The small intestine was invariably found congested and distended with whitish glairy fluid. Vibrios were isolated from the heart's blood, the small intestine, the peritoneum and the gall-bladder.

The results of the experiments are given in table I.

The table shows that early invasiveness into the general circulation occurs in the case of cholera and some para-cholera vibrios but not in the case of saprophytic Hooghly water vibrios, although eventually death may occur with all the types of vibrios. It appears probable that cholera and some para-cholera vibrios are highly invasive, whereas saprophytic vibrios are as a rule not early invasive.

Intragastric administration of vibrios into guinea-pigs.—Koch's method was followed with slight modifications. No food was given to the animals in the morning and at about 10 o'clock, 5 c.cm. of 5 per cent sodium carbonate was administered directly into the stomach by means of an ordinary long record-syringe needle the end of which had been made smooth and bulbous by fusing a piece of lead. This was done to neutralize any acid that might be present and might kill the vibrios. A few minutes later, 15 c.cm. of an 18-hour-old broth culture of vibrios was similarly given. 0.25 c.cm. of tincture of opium was then injected intraperitoneally to paralyse the gut and delay evacuation. It was found advantageous to give the opium mixed with a little atropine before the vibrios were introduced. (In earlier experiments the dose of opium given was 1 c.cm. which was found fatal even to control animals, and hence the dose was reduced.) The results are given in table II.

Post mortem, inflammatory changes and vibrios were present in the small intestine. Although it appears from the table that para-cholera and saprophytic vibrios are more virulent to guinea-pigs than the standard cholera vibrios, no significant distinction can be demonstrated by feeding experiments.

Intravenous administration of live vibrios in rabbits.—Four loopfuls of young agar culture of vibrios were suspended in normal saline and injected intravenously into rabbits. All the animals died in 1 to 2 days, showing congestion and a collection of creamy fluid in the small intestine, and vibrios were isolated from the fluid.

TABLE I

Inoculum	Number of animals for each strain	Invasiveness			Death in days						Post-mortem	REMARKS
		2 hours	18 hours	36 hours	1	2	3	4	5	6		
<i>V. cholerae</i> Inaba sub-type 3 strains												
Strain no. 1 ..	4	+	+	±	1	0	1	0	0	0	+	Mortality 50%. Tested twice at 3 weeks' interval.
" no. 2 ..	4	+	+	±	1	1	0	0	0	0		
" no. 3 ..	4	+	+	±	0	1	0	1	0	0		
Non-agglutinating (NAG) vibrios from a cholera case.												
Strain no. 1 ..	4	+	+	±	3	0	0	0	0	0	+	Mortality 62%. Only NAG vibrios were isolated from day to day from this case of cholera.
" no. 2 ..	4	—	—	±	2	0	0	0	0	0		
Hooghly water NAG vibrios.												
Strain no. 1 ..	4	—	—	±	1	0	2	0	0	0		Mortality 75%.
" no. 2 ..	4	—	—	±	1	1	1	0	0	0		
" no. 3 ..	4	—	—	±	1	0	2	0	0	0	+	

+ indicates that the small intestine was congested and contained turbid fluid; vibrios were recovered from the heart's blood, the peritoneum, the intestine and the gall-bladder.
± indicates that some animals showed vibrios and some not.

TABLE II

Old laboratory strain of vibrios	Total number of animals	Dead	Alive
Inaba sub-type ..	4	2	2
Para-cholera vibrios ..	5	5	0
Hooghly water NAG vibrios.	6	5	1

No difference in the pathogenicity of the different types of vibrios could be demonstrated.

Histological section of the intestine showed denudation of epithelium, congestion and the presence of vibrios in the submucosa.

Summary

1. *V. cholerae* and para-cholera vibrios, when injected subcutaneously in suitable doses into guinea-pigs, invade the general circulation, as a rule within 2 hours, but saprophytic vibrios found in Hooghly water do not do so so early.

2. No definite distinction can be made amongst the above types of vibrios by feeding experiments in guinea-pigs, and by intravenous injection into rabbits. All the types of vibrios produce fatal results in the animals, the non-agglutinating vibrios producing a slightly higher percentage of fatality.

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SOME ASPECTS OF TUBERCULOUS INFECTION IN SAIDAPET

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THE material for this article was collected by a tuberculosis survey unit which worked in Saidapet between July 1940 and March 1942 under the auspices of the Indian Research Fund Association.

The scope of the survey included a study of infection, morbidity, mortality and other features, and the findings have been reported in the official reports of the Indian Research Fund Association. This article is confined to certain aspects of the study. The data collected are on the lines recommended by the Indian Research Fund Association Tuberculosis Survey Committee in its report of 1940.

Saidapet is a suburb of the city of Madras and is easily reached by rail or bus in half to one hour from the city of Madras. It is a municipality which has a protected water supply but not to individual houses. Water from open wells and other sources is also freely used. There is no system of drainage. The sillage and sewage that is collected in the houses in concrete receptacles is baled into conservancy carts which the municipality employs, and is discharged within municipal limits and left untreated. Much sewage is also allowed to soak in and around the houses. There are very few public latrines, and streets and open spaces are freely fouled. The total population of Saidapet according to 1941 census is 41,385. This is distributed

in what may be described as Saidapet proper and outlying areas. Saidapet proper area has a population of 21,430.

The population is almost entirely Indian. A few foreigners also live within the municipal limits. Of this non-Indian group, three came within the purview of the survey. They were all Americans.

The composition of the population.—The main section of the population consists of persons engaged in the weaving industry. Dyeing, pot making, clothes washing and the milk trade account for the other major sections of the people. There is a fairly large section of public and domestic servants, whose work is within or outside the town. The weavers and the servants above mentioned frequently visit the city on business or pleasure, taking advantage of quick and easy transport facilities.

The bulk of the population lives in Saidapet proper, which is a small area compared with the rest of the Saidapet municipal area. Hence in Saidapet proper there is overcrowding. For descriptive purposes, reference is made to two different areas. One is called the fresh survey area where the tuberculosis investigation was made for the first time commencing from July 1940. The other area is called the re-survey area; as in this area a preliminary tuberculosis investigation was made in 1938-39. This division makes possible a comparative study of a fresh area with the findings of the previous survey.

The selection of the areas for survey.—The fresh survey area was made up as follows. From a central point in the heart of Saidapet streets all round about were taken for the study. In three of these streets an attempt was made to include every member of every house within the scope of the survey. In the other streets many of the homes were visited, and tests were done wherever co-operation was forthcoming. Eight streets far from the centre and on the fringes of Saidapet proper were also surveyed.

By the above process all topographical groups of the population were adequately represented. Further, by this process, representative occupational groups were included. Thus in one section the entire population belonged to the weaving industry. Another area was a scavenger colony. In a third area, the people worked in the milk trade. In the rest of the area surveyed, there was a generous mixture of domestic and menial servants, potters, dyers, weavers, trade and factory employees.

The re-survey area was fixed by the previous survey. The attempt was made not merely to get as many persons as possible for the test, but also to test a second time all those who had previously been tested in 1938-39. Experience of severe and unpleasant reactions as a result of the test, and a failure to obtain treatment facilities for persons who were told during the last survey that they should get treated, were responsible for the less co-operative attitude of the people in this area.

The Mantoux tuberculin test.—The Mantoux tuberculin tests and the collection of information regarding age, sex, etc., were done at the homes by regular visits made by the survey unit.

The test was done with old tuberculin (H) (supplied by Burroughs Wellcome & Co.) diluted 1 in 500 in normal saline with 0.2 per cent phenol. 0.1 c.cm. of the test solution was injected intradermally on the palmar aspect of the forearm about its middle. The dilution 1 in 500 was used as a result of experience gained in the previous survey, when many individuals who had the test with 1 in 1,000 dilution and were negative, either could not be found or refused to have a second test with the stronger dilution of 1 in 100 which it is necessary to employ before a person can be declared to be negative. The tests were given by one medical officer and read by him at the end of 48 to 72 hours.

The results of the test were divided into negative and positive. The negatives were those who showed no response except that due to the piercing of the skin by the needle, or showed a wheal or redness of insignificant dimension. The positives were grouped in four grades.

One plus (+), slight but defined oedema raised 1 mm. above skin surface with diameter not more than 10 millimetres in the largest axis.

Two plus (++), well-defined oedema raised somewhat more than 1 mm. above skin surface, diameter between 10 to 15 mm.

Three plus (+++), more extensive oedema with diameter exceeding 15 mm. and thickness exceeding 1.5 mm. above skin surface, wide area of redness beyond but no vesiculation or necrosis of the skin.

Four (++++), characterized by extensive oedema, redness, vesiculation and necrosis, possibly associated with temperature and malaise.

Findings of the Mantoux test

In all, 5,931 tests were done. Of these 3,559 or 60 per cent gave positive results.

(a) Infection according to streets

Fresh survey area.—The percentage of persons giving a positive reaction varied in the several streets. For the whole area including 31 streets, the Mantoux positives were 2,498 out of 4,160 examined, or 60.0 per cent. In no street were the positives more than 90 per cent. In only one street was the percentage over 80 per cent. Six streets had a figure from 60 to 70 per cent. The largest group of streets, ten in number, gave figures between 50 and 60 per cent. In four streets the figure was from 40 to 50 per cent. Two streets only gave a figure below 40. The highest figure for any street was 80.9 and the lowest 31.5.

Re-survey area.—This included 16 streets. In only one street were the positives over 80 per cent; in two streets the figure was between 70 and 80. In six streets the figure was between 60 and 70; this is the largest group. In four streets the figure was between 50 and 60 and in

three streets between 40 and 50. There was no street with a figure below 40 per cent. The highest figure was 81 and the lowest 41.

(b) *Infection according to age*

The tested persons were divided into two main groups, adults and children (those 15 years and below)—the relevant figures for infection according to the area are given below.

Fresh survey area.—*Adults*: Of 2,285 tested, 1,771 or 77.8 per cent gave a positive result. *Children*: Of 1,875 tested, 720 or 38.4 per cent gave a positive result.

Re-survey area.—*Adults*: Of 854 persons tested, 702 or 82.1 per cent gave a positive result. *Children*: Of 917 tested, 360 or 39.3 per cent gave a positive result.

Infection according to age groups.—For this purpose the age groups considered are—2, —5, —10, —15, —20, —30, —40, —50, —60, —70, —80 and —90. The large majority of the persons tested come under the six age groups, —5 to —40, and account for 5,339 out of 5,931, or nearly 90 per cent. The other age groups together represent only 10 per cent of the tested persons. The single age group in which the largest number of persons were tested, i.e. 1,110, is the 21 to 30 age group. This is the same age group that had the largest number of tests in the 1938–39 survey also. On an analysis of the results of the Mantoux test into the above age groups, the number of positive Mantoux reactions was found to rise progressively from 11.9 per cent in the —2 age group, to 84.8 per cent in the —40 age group. From the —40 age group to the —70 age group, there was a progressive decrease from 84.8 per cent to 66.7 per cent, but curiously enough, in the —80 age group, all the six tested were positive. Owing to the small numbers tested, no significance is attached to this finding. This progressive decrease in the Mantoux positives from the —40 age group to the —70 age group is noted particularly in the males, from 84.4 per cent in the —40 age group to 50 per cent in the —70 age group. In females the decrease is not so marked, 85.2 per cent in the —40 age group and 78.6 in the —60 age group. In the —70 and —80 age groups in the females, the numbers were too small to justify conclusions.

(c) *Infection according to sex*

This was worked out separately for children and adults in the survey area. The infection rate according to sex was also further studied in relation to specific age groups. The findings are given and discussed later.

(d) *Contacts and infection*

Infection in known contacts of open cases of tuberculosis.—The following table indicates the information with regard to contact and infection with tuberculosis.

It is seen that the open contacts show a higher incidence of positive results. Moreover the degree of reaction was enhanced.

The plus two and plus three reactors in the contact group were more than twice as common

Number examined	Percentage of positives in familial contacts of open cases	Percentage of positives in general population
Adults 83 ..	92.8	78.4
Children 47 ..	80.9	38.2
Total 130 ..	88.5	59.3

as in the corresponding group in the general population (19.2 per cent and 8.13 per cent). Those which showed a plus four reaction were nearly three times more common. The higher incidence and degree of positive reaction in open contacts were seen at all ages, but particularly in children.

Infection and contact history.—A definite attempt was made to obtain a history of contact with a tuberculous individual of all reactors who showed a reaction of plus 3 and above*. The gross results were as follows:—

Of 746 high reactors who were interrogated for the purpose, only 327 gave a definite history of contact. These contacts can be classified as intimate contact 142, close contact 108, past distant contact 77.

Even among strong reactors (3 and 4 plus) it was possible to obtain a definite contact history only in 43 per cent of cases.

(e) *Infection in relation to habitat and change of habitat*

Saidapet as stated earlier is an urban area, but there is frequent interchange of population with rural and other urban areas, as workers and property owners frequently come to and go from Saidapet in pursuit of occupation or other interests.

A study of 126 high reactors (plus 3 and above) who had moved into Saidapet during the last two years showed that 74 had come from urban areas, 45 from rural areas and 7 from semi-rural areas.

Correspondingly 155 persons tested within the last two years and showing a similar (3 or 4 plus) positive reaction, moved away from Saidapet. Eighty-two moved away to urban, 26 to semi-rural and 47 to rural areas.

In one street in the surveyed area, a special study of the movement of population and its relation to infection was made. It was found that 163 persons tested in 1938–39 had moved out of the street. These persons had given a total positive percentage of 85.9 per cent, for adults alone 89.3 per cent, and for children alone 78.4 per cent.

* Does this statement not vitiate to some extent the previous statement that in open contacts, the incidence and degree of reaction were high?—EDITOR, I. M. G.

One hundred and thirty-seven persons who had moved into this street since the last survey gave a positive percentage of 57.7. The adults had 77.9

There is no significant difference in infection rate between the outskirts and the centre of the town.

Occupation	Street number and area	ADULTS AND CHILDREN		CHILDREN		ADULTS	
		Number examined	Percentage positive	Number examined	Percentage positive	Number examined	Percentage positive
Dhobi	Re-survey area						
	11	17	82.4	9	66.7	8	100.0
	14	56	76.8	28	60.7	28	92.9
Weaving	Survey area						
	1	495	59.4	164	34.0	331	71.0
	4	277	58.8	112	35.7	165	74.5
Milk trade ..	22	169	44.4	94	25.5	75	68.0
Public scavenging ..	25	221	72.8	51	31.4	170	85.3

per cent positives and the children 23.6 per cent positives.

(f) Occupation and infection

Four group-occupations were selected for study. The persons studied in each occupational group lived in separate localities or streets. Only actual family occupations in which every member of the family had some contribution to make were considered.

Discussion

The general infection rate.—The dilution used for the Mantoux test was 1 in 500. On this routine it was found that 60 per cent were positive in the fresh survey area and in the re-survey area 59 per cent. In the 1938-39 survey, the positives were 58.1 per cent. In Madura the percentage of positives detected during a recent survey was 65 per cent which is higher than the Saidapet incidence, but a smaller group was tested and a dilution of 1 in 100 was used in cases where the reaction to the 1 in 1,000 solution was negative. In the 1938-39 survey it was found that, of 254 persons who did not react to a 1 in 1,000 strength, 125 gave a positive reaction when the higher strength of 1 in 100 was used. Thus nearly 50 per cent of original negatives were positive to the 1 in 100 dilution. Therefore it can be safely assumed that at least 10 per cent more of our negatives would have turned positive if a 1 in 100 solution had been used for a second test. On this basis the positive rates would be at least 70 per cent.

Infection according to streets.—As indicated in the findings, there is much variation in the infection rate from street to street. The accompanying table indicates the extent of infection, showing the heaviest and the least infected streets in the survey and re-survey area. This will be useful material for planning a further intensive survey in the areas, and for obtaining information likely to point to factors influencing the intensity of infection.

Streets in which infection is heavy

ADULTS AND CHILDREN COMBINED		ADULTS ALONE		CHILDREN ALONE	
Street number	Infection per-centage	Street number	Infection per-centage	Street number	Infection per-centage
(1) Fresh survey area					
15	80.9	16	100.0	15	70.7
11	77.9	17	93.3	12	59.3
17	77.2	11	91.5	16	56.3
12	75.2	15	91.2	11	61.5
(2) Re-survey area					
11	82.4	11	100.0	11	66.7
14	76.8	14	92.9	14	60.7
18	70.9	17	87.6	18	57.8
17	67.8	7	85.9	10	52.9

Streets in which infection is light

ADULTS AND CHILDREN COMBINED		ADULTS ALONE		CHILDREN ALONE	
Street number	Infection per-centage	Street number	Infection per-centage	Street number	Infection per-centage
(1) Fresh survey area					
30	31.5	30	57.1	30	16.7
28	36.7	27	66.7	29	24.6
22	44.4	22	68.0	8 and 3	26.3
29	48.3	10	67.4	22	25.5
(2) Re-survey area					
2	42.1	2	64.0	4	22.2
3	45.8	3	66.7	2	22.8
4	46.2	4	75.9	5	30.8
5	53.5	18	80.4	8	32.5

Infection and movement of population.—In an analysis of the results of the Mantoux test in 137

persons who were not living in street no. 1 re-survey area in 1938-39, but had moved into that street since then, in general it was found that those who moved away from the street were more commonly infected than those who moved into the street. This disparity in infection rate has influenced the infection rate in the street which according to the present survey is much less infected than in the previous survey*. The findings are given in the following table :—

Street No. 1, Re-survey Area
Infection rate in 1938-39 and 1940-42

Survey	ADULTS AND CHILDREN COMBINED		CHILDREN ALONE		ADULTS ALONE	
	Number examined	Positive percentage	Number examined	Positive percentage	Number examined	Positive percentage
1938-39 ..	410	84.6	164	76.8	246	89.8
1940-42 ..	249	61.4	109	34.9	140	82.1

The figure for positives in children is much lower than in 1938-39, but for adults only slightly lower.

Tuberculin reaction in relation to age.—It was found that 38.4 per cent of the population below the age of 16 had been infected in the fresh survey area and 39.3 per cent in the re-survey area.

Page! quoting from Goldberg gives the crude infection rate of children 15 years and under as below :—

Philadelphia	68.5 per cent
Minneapolis	47.3 " "
London	43.1 " "
San Francisco	23.5 " "

Our figures are lower than the first three. It is also well to remember that in all these cities well-established clinics and anti-tuberculosis measures have existed for a long time. In Sialkot in India, in a recent survey of school children between the ages of 5 and 18 Dr. Sahni found 33.6 per cent to be the infection rate.

In the fresh survey area, it was found that 12 per cent of the children are infected before they are 2 years old, that the rate is doubled when the age of 5 is reached, trebled by the time 10 years is passed, and multiplied by 5 when the children reach 15 years of age. Hence the data collected indicate that the process of 'tubercularization' is rapid in childhood.

The study in Saidapet 'therefore indicates a serious situation with very early infection. It also indicates that the infection takes place

mainly before the children are much in contact with the outside world. It points rather to serious home or possibly school infection, which requires further investigation'. One cannot easily dismiss the implied suggestion that with growing years the child's contacts increase and thus the chances of infection also increase. The big jump in infection rate in the later years of childhood may also be accounted for by this.

Infection according to age and sex.—The findings are given in the following tables :—

Sex	Fresh survey area	Re-survey area	1938-39 survey
<i>Adults and children considered together</i>			
Males ..	62.4	61.3	60.2
Females ..	57.8	58.7	57.7
<i>Adults alone</i>			
Males ..	80.5	82.7	69.7
Females ..	75.2	81.5	68.3
<i>Children alone</i>			
Males ..	39.6	42.0	42.5
Females ..	37.2	36.8	36.3

It is seen that in all surveys in both areas, both in childhood and adult life, the infection rate in males is higher than in females. The difference is sometimes slight and never very marked but nevertheless is probably significant.

As the following table shows however, this difference is not seen in early infancy, when the female rate exceeds the male rate in all the surveys. In individual surveys in one or more but varying groups, the female rate slightly exceeded the male rate. These were probably chance findings.

Infection according to age groups in the two sexes

Age	FRESH SURVEY AREA		RE-SURVEY AREA		1938-39 SURVEY	
	Males	Females	Males	Females	Males	Females
- 2	8.0	15.2	12.0	14.3	36.9	38.5
- 5	23.5	21.7	21.5	18.8	29.8	29.4
-10	35.7	32.7	40.9	35.6	41.4	38.4
-15	59.7	58.0	61.8	52.6	44.0	38.0
-20	72.7	65.1	70.8	69.6	61.6	64.6
-30	82.1	72.9	83.1	81.6	68.4	67.8
-40	84.4	85.2	91.4	89.9	73.0	69.4
-50	82.7	85.2	89.2	91.2	76.8	71.7
-60	82.9	78.6	78.0	87.5	100.0	71.4

Agés above 60 are not considered as the numbers are meagre.

Infection and occupation.—In the table relating to occupation it will be observed that dhobi

* This statement presupposes that this migration is a new or a markedly increased factor since 1938-39. It seems doubtful if this is so.—Editor, I. M. G.

children are more infected than children living in homes where the other occupations are pursued. Next in order comes weaving. The third is public scavenging and the least infected are children in houses engaged in the milk trade.

In adults, the occupation of dhobi takes the first place; next comes public scavenging; weaving takes the third place. The last here also is the milk trade.

Although it must be admitted that definite conclusions cannot be arrived at from the above findings, there is here an indication for further investigation of the occupation of a community in relation to infection.

Summary

The paper deals with certain aspects of tuberculous infection in Saidapet.

The area selected is briefly described, and note is made of the condition of communications, water supply, drainage and public sanitation as also special medical relief.

The manner of selection of areas for the Mantoux test is mentioned and the technique adopted is described.

The results are analysed in both the fresh and the re-survey areas, and compared wherever possible with findings of the 1938-39 Saidapet survey. Infection is studied in relation to its distribution in the various streets surveyed, in relation to age, the population being first divided into adults and children and then into various smaller age groups. Infection according to sex is next studied. Other items of the findings relate to the influence of contact on the results of the Mantoux test.

A study of movement of population and its influence on the infection in one street that was surveyed in 1938-39 and again 1940-42 is made.

A study is made of infection in four occupational groups.

Finally four streets are indicated in which there is a heavy infection rate and also four other streets where the infection is least, for a further intensive study of the factors which tend to produce the difference in the infection rate.

Acknowledgments

We have much pleasure in expressing our gratitude to Dr. P. V. Benjamin for his sustained interest and guidance throughout the investigation. He has also very kindly allowed the use of information collected by him in the 1938-39 survey. We are also extremely grateful to Dr. G. Rajagopalan, Medical Officer, Silver Jubilee Clinic, Saidapet, for assistance readily given, and to the Madras Provincial Branch of the British Empire Leprosy Relief Association for permission to use the laboratory and other facilities at the Silver Jubilee Clinic. We also gratefully acknowledge the assistance of the Indian Research Fund Association and the Madras Government without whose aid it would have been impossible to undertake this investigation.

THE ADMINISTRATION OF SULPHUR THROUGH DRUGS AND FOODS IN THE COURSE OF SULPHONAMIDE THERAPY

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It has generally been considered unsafe to give onions, eggs and other sulphur-containing foodstuffs, as well as medicines containing sulphur, to a patient who is receiving the sulphonamide group of drugs. It has been said that the sulphur moiety may lead to sulphæmoglobinæmia which causes cyanosis; the sulphæmoglobin, not being reconvertible into hæmoglobin, reduces the oxygen-carrying capacity of the blood. Archer and Discombe (1937) suggested that only one or two eggs should be taken daily, and that aperients should be forbidden. They particularly forbade magnesium sulphate. The work of Richardson (1941) on mice leads one to conclude that foods containing sulphur are more likely to produce sulphæmoglobinæmia. An editorial (1941) in the *Lancet* concluded 'clinical experience suggests that provided purgatives are avoided, sulphæmoglobinæmia is rare with sulphanilamide therapy even without restriction of diet'. Smith (1940), as a result of a studying of a small but carefully controlled series, feels that patients receiving sulphapyridine can safely be given pentothal and magnesium sulphate at the same time.

The present study was undertaken to ascertain by clinical methods if there was really any danger of producing cyanosis, and, even if it was produced, whether there was any serious damage to the health of the patient.

Plan of work.—Alternate cases of lobar pneumonia on sulphonamide therapy were given sulphur, either in the diet or as a purgative in the form of magnesium and sodium sulphate; the presence of cyanosis was looked for as evidence of sulphæmoglobinæmia; the dosage and the administration of the drug were controlled carefully.

Clinical material was made available by the courtesy of the Officer Commanding, British Military Hospital, Jhansi, and the authorities of the Cantonment General Hospital, Jhansi; five private cases have also been included in the series.

The plan of treatment adopted in all the cases was simple and, as far as practicable, uniform. The patients were nursed in the verandah day and night, being screened from direct sunlight and inclement weather whenever necessary. Fluids were given freely, at least three and a half pints being given in twenty-four hours, and sulphapyridine (M.&B. 693) was administered according to the under-noted dosage.

First dose, 4 tablets. Second dose, 4 hours, later, 4 tablets. Third and subsequent doses, 2 tablets every four hours, including sleeping hours, until the temperature touched normal and

remained so for twenty-four hours. Then 1 tablet was given every four hours for twenty-four hours, and then 1 tablet every eight hours for another twenty-four hours.

An average of 24 to 28 grammes was given in each case. All the cases recovered without any complication, and convalescence was uneventful. The diet consisted of glucose 7½ per cent with lemon or orange juice to flavour, tea, milk, cocoa, ovaltine and biscuits. Alternate patients each received two to four eggs daily as the source of sulphur; 38 cases were studied in this series and the results are here given.

Number of cases treated in the series	Number receiving sulphur in diet	Cyanosis noted in
38	19	0

Four of the 19 cases in column two also received a purgative during the febrile period, consisting of 120 grains of magnesium sulphate and 60 grains of sodium sulphate in one ounce of warm water. Cyanosis as mentioned above, was not noticed in any of the four cases. Purgation was undertaken only as a method of giving sulphur to the patients, and not as a therapeutic measure.

Experience with the above cases gave one sufficient confidence to try the experiment on other cases. A series of 14 surgical cases was therefore studied. The diet included two to three eggs, and onions, and each patient had at least two purges during the course of treatment, one by means of magnesium sulphate and the other by means of senna. Eleven cases received sulphanilamide tablets only, and the remaining three cases received prontosil album by mouth and prontosil rubrum by injection. Cyanosis was not seen in any of the cases. Treatment in this series was not as uniformly successful as in the first series, but the absence of cyanosis proved the harmlessness of giving sulphur conjointly with sulphonamide.

Discussion.—As cyanosis had been reported under similar conditions, it was considered necessary to find out an explanation for the results in the present experiment. Sulphur is produced in the human body as a result of the breaking down of food products and also as a result of endogenous metabolism. During fever, the rate of endogenous metabolism is higher than in normal health, and therefore the amount of sulphur produced during fever will be greater than in health. The two or three eggs in the diet cannot add very much to the amount of sulphur thus produced, and therefore cannot contribute much to the production of cyanosis. In any case the human body is well adapted to take care of slight variations.

Again, magnesium and sodium sulphates act as purgatives by virtue of their drawing water out of the intestine without themselves being absorbed from the intestinal canal. They

cannot act as purgatives and also cause cyanosis at the same time. A likely explanation of cyanosis under these circumstances is this. The normal intestinal flora can deal with any sulphur produced in the intestine and prevent its absorption into the blood, thus preventing cyanosis. Purgation upsets this flora violently—exactly how and to what degree is being studied—and as a result, the disturbed flora cannot deal with all the sulphur; and it thus allows some of it to be absorbed into the blood causing or tending to cause cyanosis. The same mechanism will hold good with any other purgative. It is therefore the purging and not the sulphate that is responsible for the cyanosis, and what should be avoided is all forms of purgation. However the experience with the 14 surgical cases would seem to indicate that even ordinary purgation need not necessarily produce cyanosis.

Case 23 developed hæmaturia but no cyanosis. He had not any onion or purgative, but had had two eggs daily until the fourth afternoon of the treatment, when hæmaturia was first noticed. Discontinuance of the drug relieved the symptoms in 36 hours, and the recovery from pneumonia was not hindered in any way by the slight deviation from the routine treatment caused by the cessation of the drug before the full usual course had been given.

The exact mechanism of the production of this hæmaturia is unknown, but as the condition can occur under various circumstances and in the absence of sulphur, the fault probably lies in the red blood corpuscles themselves, and not in any drug. In any case the slight amount of methæmoglobinæmia present in the above case was not sufficient to produce any cyanosis.

This is admittedly a small series but war conditions have not allowed a wider study. It is, however, submitted that sufficient data have been produced to warrant a wider scale experiment with larger doses of sulphur.

Lieut.-Colonel H. S. Rajan, I.M.S., has helped me in this study by constant encouragement. I wish to express my thanks to him.

Note.—Since the above was written a case has come to notice where the above form of treatment of lobar pneumonia had been adopted and all forms of sulphur strictly avoided. This case developed hæmaturia on the fifth afternoon of treatment and simple discontinuance of the drug relieved the condition in three days. Recovery from pneumonia was complete and convalescence uneventful.

Summary

1. The advisability of giving sulphur in any form concurrently with sulphonamides to a patient has been studied.
2. Two series of cases have been studied and no cyanosis has been noticed in either.
3. Possible explanations have been offered of the fact that sulphur given in diet or drug

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PARENCHYMATOUS KERATITIS FOLLOWING RIBOFLAVIN (VITAMIN B₂) DEFICIENCY

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Introduction

RIBOFLAVIN or vitamin B₂ (no. 1), a definite member of the 'vitamin B complex', is a pigment of the flavin type and has the empirical formula C₁₇H₂₀N₄O₆. It has also been called vitamin G, lactoflavin and ovaflavin. The other vitamin B₂ (no. 2)—the P-P factor, nicotinic acid—has the formula C₆H₄N COOH, and its amide, C₆H₄N CONH₂.

Riboflavin has been isolated in pure form from liver, yeast and milk, and it has also been prepared synthetically. The crystals of riboflavin are orange yellow in colour, and are soluble in water. The yellow watery solution is fluorescent in ordinary light. It is not affected by atmospheric oxygen, but it takes up hydrogen from reducing agents and easily gives up its oxygen. It has been established beyond doubt that riboflavin plays an important rôle in the oxidation process of cells.

In 1932 Warburg and Christian reported on a new oxidation enzyme, present in animals and plants, which later was found to be identical with vitamin G, now known by the non-proprietary name 'riboflavin'. This enzyme is probably present in all living cells, and is concerned with the chemical reactions involved in cell respiration. As it is so important for the living cells, it must be supplied in adequate quantity in the diet. In the complete absence of riboflavin, death occurs due to cellular asphyxia resulting from lack of the catalyst for cellular oxidation.

Recent studies indicate that riboflavin is present in the eye and probably plays an important rôle in various ocular affections.

Ocular lesions in experimental animals

A specific association of conjunctival and corneal lesions with riboflavin deficiency in man apparently had not been noted prior to the year 1939. Previous to this from 1926 onwards, several workers (Day, Langston and O'Brien, 1931, and others) reported on the clinical manifestations in experimental animals (rats) on diets deficient in riboflavin. These mainly consisted of alopecia around the eyelids and excessive lacrimation. Pappenheimer reported on the

histological examination of the cornea of one of these rats and found 'a very slight keratitis and some new-formed blood channels'. Day, Langston and O'Brien reported in 1931 on ocular changes in 37 rats fed on a diet deficient in riboflavin. In addition to alopecia, lacrimation and conjunctivitis, they found anterior interstitial keratitis in 100 per cent, and cataract in 94 per cent. In most cases, the cornea showed superficial vascularization. Microscopic examination revealed an inflammatory process in the anterior stroma. The epithelium was normal but there was sub-epithelial, small lymphocytic and leucocytic infiltration accompanied by new blood vessel formation.

Four years later, in 1935, Bourne and Pyke in similar experiments were able to produce cataract in only 31 per cent of the animals after a period of 79 days on the diet, and they stated that the most consistent ocular symptom was 'superficial keratitis' which occurred in 92 to 100 per cent of the rats within 70 days.

Bessey and Wolbach (1939) made a detailed study of the vascularization of the cornea in rats fed on a diet deficient in riboflavin. They state 'vascularization of the cornea is an early and constant phenomenon in albino rats in riboflavin deficiency. It precedes all other demonstrable lesions of the deficiency'. The first evidence of corneal vascularization takes the form of sub-epithelial radial ingrowth of capillaries from the limbus. Later, they encroach towards the centre of the cornea and some of the blood vessels invade the deeper layers of the stroma. Cloudiness of the cornea develops only several days or weeks after vascularization has occurred. The corneal epithelium remains unaffected until late in the deficiency state.

It has been suggested by Bessey and Wolbach that the vascularization of the cornea in experimental riboflavin deficiency is a response to asphyxiation of the corneal stroma, which view has been supported by Johnson and Eckardt (1940). Riboflavin forms an essential constituent of the oxidation system of Warburg's yellow enzyme. In an avascular structure, such as the cornea, oxidation within the cells is accomplished by Warburg's yellow enzyme. Hence, when riboflavin is absent or deficient, the oxidation system of the cornea is seriously impaired. The sub-epithelial proliferation of blood vessels from the limbus into the cornea is possibly an attempt by the cornea to overcome local asphyxia by bringing in O₂ in the blood in closer proximity to the corneal cells. When riboflavin is supplied in sufficient quantity, intracellular oxidation takes place normally, following the restoration of the Warburg's yellow enzyme system, and regression of the blood vessels from the cornea takes place.

Clinical riboflavin-deficiency syndrome

In 1940 Kruse and others reported on ocular symptoms of 9 patients with clinical ariboflavinosis. Most of them had cheilosis and

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together with sulphonamides does not produce sulphæmoglobinæmia.

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glossitis and 33 per cent had seborrhœic accumulation at the naso-labial folds. Five of the patients had marked circum-corneal injection and gross opacities in the cornea. Slit lamp studies revealed sub-epithelial proliferation of blood vessels from the limbus at the nasal and temporal sides of the cornea. Later the capillaries invaded the substantia propria of the cornea, and superficial and interstitial infiltrations appeared. Nicotinic acid, thiamin, cevitamic acid, cod-liver oil or crystalline vitamin A had no effect on these corneal lesions, but riboflavin caused a regression of the lesions, characterized by improvement in subjective symptoms, diminution in size and occlusion of the capillaries, and by resolution of superficial and interstitial infiltrations. Recently, Cosgrove and Day (1942) reported on 28 patients with corneal diseases treated with riboflavin. The results varied considerably. Cases of interstitial keratitis associated with hereditary syphilis responded much more rapidly when riboflavin was administered than when anti-syphilitic treatment alone was given. Possibly these cases are a mixed nutritional and syphilitic keratitis rather than a true syphilitic one. Some cases of keratitis of unknown ætiology responded miraculously upon the addition of riboflavin to the diet. Allergic cases did not respond.

Lately some cases have been reported with involvement of the cornea, angular stomatitis, fissuring of the tongue and scurfiness of the skin of the scrotum (oro-oculo-genital syndrome), which have responded very well to riboflavin therapy.

Case report

P. N. R., Hindu male, aged 30 years, a partial albino, came into my consultation room on 1st January, 1943, complaining of rapid failure of vision in his left eye.

Present history.—About 2 months ago his left eye became slightly red and he could not stand the light. There was no discharge from the eye and no sticking of the lids in the morning. He consulted an eye specialist and was under his treatment for 2 months, but the eye grew worse and he was now practically blind in his left eye.

Past history.—Nothing particular.

On examination.—Right eye—normal. Pupil active to light. Tension—normal. Vision 6/6.

Left eye—circum-corneal injection. Slight ptosis and enophthalmos on account of photophobia.

Cornea—almost totally opaque. On oblique illumination, the whole of the cornea is marked in its deeper layers by vertical lines with offshoots and small punctate opacities. There is no new blood vessel formation in the cornea. The pupil can hardly be seen.

Vision is reduced to perception of light only, tension is normal, and the fundus cannot be seen.

Slit lamp examination.—The corneal epithelium is healthy and not affected. The deeper layers of the substantia propria as well as the anterior stroma are infiltrated and marked mostly by vertical white lines with offshoots and less by small white punctate spots. No blood vessel could be seen in any part of cornea, whether in the anterior stroma or in the deeper layers. The endothelium had lost its sharp outline and looked hazy. There was no punctate keratitis.

General examination of the patient revealed that he had slight angular stomatitis and slight fissuring of the tongue. The skin of the scrotum was normal. The diagnosis of parenchymatous keratitis due to riboflavin deficiency was made. No Wassermann test was done.

Diet.—The patient takes an average Bengali diet consisting of rice, dal, fish, eggs, vegetables, milk, etc.

Treatment.—The patient was put on atropine ointment 1 per cent to keep the pupil fully dilated. Total dose of lactoflavin (Roche) administered is 100 mg., by intramuscular injection 60 mg.; by mouth 40 mg. The average daily dosage was 4 mg.

Progress of the case

Angular stomatitis and fissuring of the tongue disappeared after 15 mg. given by injection. The whole of the cornea cleared up after 29 days, and vision was restored to 6/6. The mode of clearing of the cornea was interesting. After about 7 days, the periphery of the cornea cleared up and circum-corneal injection was very much less, but the centre of the cornea was still opaque with vertical lines and dots. After about another 7 days, the centre of the cornea started clearing up. The vertical lines became fragmented, offshoots became scarce, and dots became much more numerous. Later, the vertical lines totally disappeared and dots were mainly confined to the pupillary area of the cornea. Anyone seeing the case at that time might have mistaken these dots for the spots of superficial punctate keratitis. After a few days, these spots also cleared up, leaving the cornea crystal clear with a vision of 6/6.

Summary and conclusions

A case of parenchymatous keratitis due to riboflavin deficiency is described. The case is unusual in that there were no new blood channels in any part of the cornea; this is supposed to be one of the essential features of corneal disease due to riboflavin deficiency. Moreover, the infiltrations were much more marked in the deeper layers of the substantia propria than in anterior stroma, whereas it has usually been held that infiltrations usually start and are much more marked in the anterior than the posterior part of the stroma. As is usually the case, the epithelium was not affected.

The clinical picture of this case differed considerably from that of syphilitic interstitial keratitis. No arsenic or bismuth injections were given and the diagnosis of nutritional parenchymatous keratitis was fully established by the clinical cure by administration of vitamin B₂.

The method of clearing up of the cornea points to the fact that the part of the cornea which is nearer the blood vessels clears up first. The cornea also gets its nutrition partly from the aqueous. Riboflavin circulates in the blood and is therefore also present in the aqueous, which takes up hydrogen from the reducing agents and thus maintains the nutrition of the cornea. The periphery of the cornea receives its nutrition from the limbal blood vessels and aqueous, and therefore clears up first, whereas the centre of the cornea has to depend only on the aqueous, where possibly the riboflavin is less, and therefore that part of the cornea is rather slow in clearing up.

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A Mirror of Hospital Practice

AN UNUSUAL FRACTURE

By M. S. MAHMOOD

Divisional Medical Officer, N. W. Railway, Rawalpindi

A GANG-MAN, aged 34 years, was brought on a stretcher to the out-patients' department for pain in the left knee joint and inability to move it, or stand on it.

History.—As stated by the patient, he ran to attend to his roll-call when his foot slipped and he fell down on his knees injuring the left knee joint.

Physical examination.—Diffuse swelling of the left knee joint, slight local rise of temperature, and rigidity of the muscles around it. Marked signs of fluid in the joint. The movements were very painful and limited. There was no marked tenderness of its bony points.

X-ray examination revealed two linear vertical fractures through the condyles of the femur and extending to the junction of lower third with the upper two-third of the shaft (see plate VIII).

Treatment.—The knee was bandaged and put on a back splint for six weeks. The patella was moved daily by the hand to prevent ankylosis. The swelling of the knee gradually disappeared and after six weeks the back splint was removed and the limb was put daily on an iron bar for flexing the knee. Such exercises were given morning and evening, and within a fortnight full movements of flexion and extension were restored. Two weeks later the patient was advised to walk with the help of crutches, which he used for about three weeks, and then he began to walk normally.

Points of interest

1. Clinically this type of fracture was never thought of; only x-ray examination revealed it.
2. Since the line of fracture passed through the condyles of the femur, which are in the joint capsule, bony ankylosis was expected, but it did not occur.

I am indebted to Dr. C. D. Newman, Chief Medical and Health Officer, N. W. Railway, for kindly allowing me to report this case.

AN EARLY CASE OF PELLAGRA

By N. C. DEY, M.B., B.Sc.

PELLAGRA is not common in Bengal where the staple food of the general population is rice. It is difficult to detect early cases, as the signs and symptoms are not pronounced. It has been rightly pointed out by Napier that 'if medical officers in India were more familiar with the signs and symptoms of pellagra, it is probable that more cases should be diagnosed'. I had the opportunity to treat a patient with early skin manifestations of pellagra but with few gastro-intestinal and nervous manifestations.

A Bengali widow, aged 79 years, had suffered several family bereavements within a very short time. She was taking sun-dried rice once a day, and was fasting frequently. She was practically without food for three or four days in a week.

On the 12th March, 1942, I was called to see this patient. She complained of intense itching sensation all over the body. Erythematous patches were seen on the radial side of the wrists, dorsum of the feet and lower parts of the legs. The patches were almost symmetrical and oval, varying from one to two inches in length, with erythematous spreading margins, superficial scaling and slight pigmentation, but without any atrophy of the skin.

A few days later, she developed numbness of the tongue and itching between the fingers and toes with thickening of the skin of these parts and of knuckles. She gradually lost her appetite and the sense of taste became impaired. There were denudation of the epithelium and fissures on the dorsum of the tongue. She did not complain of any other gastro-intestinal symptom except slight diarrhoea occasionally.

Except general irritability of the skin, a feeling of depression, and occasional giddiness and insomnia, there was no nervous symptom. The depression was sometimes marked and the patient felt morose and prostrated. There were a slight tremor of the tongue and weakness of the limbs. The knee jerk was normal.

The blood pressure was 110/80.

The blood picture—red cells 2,480,000 per c.mm., white cells 6,400 per c.mm., lymphocytes 32 per cent, monocytes 6 per cent, polymorphonuclears 60 per cent and eosinophils 2 per cent. Hæmoglobin 51 per cent (Hellige).

Treatment.—The patient was advised a balanced diet. Calamine liniment was applied locally when there was itching or irritation. She was also given a course of nicotinic acid, two tablets 50 mg. each twice a day, followed by one tablet three times a day for the next week.

As the patient improved, she began to have pain in the epigastrium after taking the tablets. The pain was so severe that the patient refused to take any more. Livogen (liver extract with yeast, nicotinic acid, etc.) B.D.H. was therefore prescribed, two teaspoonsful three times a day after meals. The patient improved within three weeks with this treatment, but then showed signs of recurrence which was however controlled by proper dieting and medicine. The patient has been well since July.

In this case the following points are of interest:—

1. The patient developed mild symptoms of pellagra due to food deficiency.
2. The skin manifestations developed earlier and were more marked than gastro-intestinal and nervous symptoms.
3. The symptoms subsided after the administration of nicotinic acid followed by liver extract.
4. The patient developed intolerance to nicotinic acid.

PRODUCTION OF SERUM IN INDIA

To meet the emergency caused by the cessation of supplies of serum and vaccines from abroad during the last World War, certain distinguished medical practitioners in Calcutta made an attempt to produce sera in this country in the year 1919. It was a tremendous task, but with the zeal, skill and abilities of the local research workers; the industry developed and expanded in such a way that sera are now being produced in quantities suitable for all purposes and satisfying as to the correct conditions and standards. The country is now in a position to supply its demand not only for the civil population but also for the military requirements. Of course, in carrying out this work tremendous difficulties, such as problems of temperature, climate and other environmental factors, have to be encountered. But all these are dreams of the past.

Still newer questions arise, and these are to be solved. Serum with high potency and less protein content is in demand. The people nowadays are not only satisfied with passive immunization but are more keen in protecting themselves by active immunization. For all these the whole art of immunology is taking a newer orientation with the development of knowledge and advancement of science. All the characteristics of toxins, antitoxins, and toxoids are being thoroughly studied to afford a product that would really help in ameliorating the conditions of the suffering public. For these the different laboratories—serological, bacteriological, biochemical and biophysical—are to be fully developed with all necessary appliances, such as ultracentrifuge, van Slyke apparatus, electro-dialyser, ultrafilter, etc., etc. All these with proper men at the proper place would help in the solution of the problem for which India clamoured during the last war. A visit to Bengal Immunity Laboratory would show how various types of sera and toxoids are being produced in quantities to meet the requirements of the physicians at the hospitals, clinics and chambers.

In one section of the Laboratory would be heard the peculiar hissing sound of various animals reared and nurtured for controlling and standardizing the production of the sera. In another part would be found the huge animals—the horses—standing erect to offer their blood for the welfare of humanity. One would then enter into the Laboratory proper where again various sections would be found working with their respective types of deadly micro-organisms. Finally one wonders in going through the control section where the different workers are recording their data after scrutinizing the purity, correctness, potency and sterility of different preparations.

The science of serum therapy is still to be further rationalized. Often a passive immunization, often an active immunization, often a synergy treatment is followed, but the problem remains untouched, how the bacterial toxins alter the body proteins, and how those body proteins again resist the attacks of the deadly micro-organisms. Much is being done for the last two decades in the Laboratories of Bengal Immunity, but an all-out drive is what is now wanted for the solution of this vast complex problem.

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Indian Medical Gazette

APRIL

TREATMENT OF KALA-AZAR: THE PRESENT POSITION

For over twenty years, the pentavalent antimony compounds have been used in the treatment of kala-azar with excellent results. During recent years, reports have been published in this journal and elsewhere on the use of certain new preparations which do not contain antimony, *viz*, the aromatic diamidines, and excellent results have been obtained in the treatment of kala-azar by these compounds. From these reports, some readers may have formed the idea that the pentavalent antimony compounds may be replaced by the newer drugs. We feel that such idea is unwarranted, at least as far as the treatment of Indian kala-azar is concerned, and we propose to examine the claims of these newer remedies *vis-à-vis* the pentavalent antimonials.

The synthesis of the aromatic diamidines and their successful application to certain protozoal infections in animals, and ultimately to the treatment of visceral leishmaniasis and trypanosomiasis in man, are the results of undoubtedly brilliant chemotherapeutic research. Of these compounds, 4:4' diamidino-stilbene, 4:4' diamidino-diphenoxy-pentane, 4:4' diamidino-diphenoxy-propane have been tried in the treatment of kala-azar by different workers. The first of these compounds, *viz*, diamidino-stilbene, has been most extensively used, and reports on its remarkable curative action in visceral leishmaniasis have been published from England (Indian cases), Palestine, and the Sudan, in different journals abroad and from India in this journal during the last three years. Diamidino-diphenoxy-pentane has been used in a smaller number of cases of kala-azar abroad. This issue of our journal contains a preliminary report on its use in 32 cases of Indian kala-azar. Diamidino-diphenoxy-propane has been tried in so very few cases that it is not possible to assess its value as an anti-kala-azar drug; and we do not intend to include this compound in our discussion.

From a review of all the available literature concerning the first two diamidine compounds, it appears that diamidino-stilbene has the more powerful therapeutic action against kala-azar. It has been found to have an immediate cure rate of 95 to 98 per cent in a series of cases treated in the Sudan and India—figures that are at least as good as those obtained in the treatment of Indian kala-azar with pentavalent antimonials. Also this compound has been found to have an almost equally powerful curative action on antimony-fast, 'resistant'

kala-azar cases. Diamidino-diphenoxy-pentane has also been found to possess a well-marked curative action in kala-azar, both in the Sudan and India; but it is less efficient than diamidino-stilbene. In the Sudan, it has an immediate cure rate of 75 per cent; in India the rate is slightly higher, but failure is not unknown, and some cases of relapse have been reported.

The administration of diamidino-stilbene produces immediate unpleasant reactions—in the majority of cases—and troublesome neuropathic sequelæ in some cases, full details of which were published in this journal (Napier and Sen Gupta, 1942) last year. It is true that the immediate reactions are generally transient, to some extent avoidable, and entirely curable by the administration of adrenalin, but the fact that they are generally unpleasant to the patient and occasionally very alarming to the physician administering the injection, precludes the routine use of this drug in an out-patient clinic where large numbers of ambulant cases have to be treated. Also the neuropathic sequel, though not dangerous to life, is quite unpleasant to the patients, and the medical practitioner might well feel hesitant in treating all cases of kala-azar with this drug. Diamidino-diphenoxy-pentane is undoubtedly more 'benign' as far as reactions are concerned, but it is less efficient as a curative agent. Also intramuscular injections of both these compounds, though free from immediate reactions, are too painful to be adopted as a routine mode of administration.

On the other hand, the pentavalent antimony compounds have been found to cure about 95 per cent of cases in India, and are noted for their ease of administration and the extreme rarity of unpleasant reactions. A small proportion of cases, however, prove refractory to these antimonials—the 'resistant' cases. These patients, after several courses of treatment, ineffective or causing but short-lived improvement, get discouraged and go home to die of complications or intercurrent disease. In the Sudan, the antimonials have apparently not been as successful in the treatment of kala-azar as in India. Stephenson found that of 54 cases of Sudan kala-azar, only 12 survived after a period of two to three years, in spite of repeated courses of injections of compounds such as neostibosan, tartar emetic and anthiomaline.

From the above discussion it will be evident that, as far as India is concerned, the large majority of ordinary cases of kala-azar will continue to be treated and cured with pentavalent antimony compounds. But, for the treatment of those cases that do not respond to pentavalent antimonials (the 'resistant' cases) whether in India or in the Sudan, diamidino-stilbene appears to be the drug of choice. Because of unpleasant reactions, the use of this drug will probably have to be restricted to hospital cases and cases in private houses where all precautions can be adopted. As for the

chance of development of the neuropathic sequel, we feel that in the treatment of 'resistant' cases, it is justifiable to use diamidino-stilbene and risk a sequel, for the chances of recovery in the 'resistant' cases are very poor with antimonials, and diamidino-stilbene has been found to have a curative action in such cases almost equal to that seen in ordinary cases.

In conclusion, we must emphasize that the aromatic diamidines will not replace the pentavalent antimonials in the treatment of the ordinary cases of Indian kala-azar, but that in diamidino-stilbene we have a remedy which holds out the best chances of cure in cases in which the antimonials have failed.

P. C. S. G.

Special Article

FRACTURES AND DISLOCATIONS OF THE VERTEBRÆ, WITH A REPORT ON FIFTY CONSECUTIVE CASES*

By G. E. DUNKERLEY, M.B., B.S. (Lond.)

Assistant Medical Officer, Kolar Gold Field

FRACTURE of the spine is as old as man's physical activity. Although head injuries appear to have engaged the attention of the earliest surgeons much more than spinal injuries, Keen (1906) records the fact that Galen (131-201 A. D.) appreciated the condition of injury to the spine with compression of the cord, made a proper diagnosis, and advised operation for relief. It is only in recent years, however, with the advent of radiological examination, that it has been recognized that many vertebral fractures occur without spinal cord damage, and more recently still has their mechanism been elucidated and satisfactory methods of reduction evolved. This is mainly due to a better understanding of the compression fracture of the vertebral body, and to the improvements in treatment of this fracture suggested by Davis (1929) and Jones (1931).

Before this, unless there was associated spinal cord injury, many fractures probably passed unnoticed, since it is necessary even now to stress the importance of taking a lateral skiagram in a case of suspected vertebral injury. Moderate degrees of compression are not revealed clearly by the antero-posterior view alone. It is not sufficiently well known that comparatively trivial violence may lead to compression of the body of a vertebra, and that only by good quality skiagrams can this lesion be excluded when a patient complains of pain in the back after an appropriate injury. It was the author's experience, when this type of case was first met with, that minor degrees of compression fracture were occasionally diagnosed only when the patient complained of persistent back pain on becoming ambulant after the injury. The misleading cases are likely to be those associated with multiple wounds and abrasions. The severity of

the accident may not be great, and at first the physical signs appear insufficient to warrant the precaution of a radiological examination.

That many fractures of some severity remained unobserved in the past is proved by the general acceptance of the existence of Kummel's disease, thought to be a rarefying osteitis of the vertebral body. At a variable period after an injury the patient complains of severe back pain, and sometimes symptoms of compression of the spinal cord appear. The skiagram shows a wedge compression of the body of a vertebra. Kummel later thought that the disease was actually a sequel of an unrecognized crush fracture, and that is the commonly accepted view at present.

Anatomy

A brief account of the anatomy of the spine is necessary to help in the understanding of the fractures to be described.

Fractures of the sacrum and coccyx are not considered in this paper. The remaining twenty-four vertebrae, although modified to serve special functions at various levels, each consists of a body and a vertebral arch enclosing the vertebral foramen. The vertebral body is roughly cylindrical in shape, with flat upper and lower surfaces giving attachment to the inter-vertebral fibro-cartilage. The vertebral arch consists of a pair of pedicles and a pair of laminae, and gives rise to four articular processes, two transverse processes, and one spinous process. The pedicles, which connect the bodies with the laminae, are short, stout bones, concave above and below. These concavities, or vertebral notches, when articulated, form the inter-vertebral foramina through which the spinal nerves and vessels pass. The laminae are broad plates directed backwards and medially, fusing in the spinous process posteriorly. This process is directed backwards and downwards and serves for the attachment of muscles and ligaments. The articular processes, two above and two below, arise from the junctions of the pedicles and laminae. The articular surfaces of the superior processes are directed backwards and medially, whilst those of the inferior processes are directed forwards and laterally. The transverse processes project laterally from the junctions of the pedicles and laminae, and serve for the attachment of muscles and ligaments. In the thoracic region, they articulate with the ribs.

The body of a vertebra consists of cancellous bone covered by a thin layer of compact bone. The vertebral arch consists chiefly of compact bone.

The inter-vertebral discs unite adjacent vertebral bodies. Each disc consists at the periphery of layers of fibrous tissue and fibro-cartilage forming the annulus fibrosus which is closely adherent to the thin cartilage plates on the upper and lower surfaces of the vertebra. In the centre is the nucleus pulposus, a yellowish highly elastic pulp, consisting of angular cells in a fine fibrous matrix.

*The original manuscript contained much more detailed case-records and had more illustrations. To facilitate publication, the details are reduced, and put in the form of several small tables. This was done by the author at the editor's request.—EDITOR, I. M. G.]

Types of fracture

Any of the parts of a vertebra, the body, muscular process, lamina, pedicle or articular process, may be fractured singly or in combination, and the signs, symptoms and treatment will vary accordingly. In mild fractures, the disc is undamaged, but in severe fractures, especially when the body is comminuted, the fibres of the annulus are torn and the nucleus pulposus may be extruded.

Platt (1938) points out that the majority of fractures and dislocations of the spine occur at the three levels of greatest mobility, upper cervical, lower cervical and dorso-lumbar. There is a remarkable preponderance of fractures at the latter site in the author's cases.

Fracture of the vertebral body

Three factors influence the type of fracture met with:—

- (1) The comparatively soft nature of the vertebral body.
- (2) The relative strength of the vertebral arch.
- (3) The strength of the anterior longitudinal ligament.

These factors result in a tendency for the body of a vertebra, when compressed, to collapse into a wedge with its apex anteriorly. The cancellous body easily collapses in front, but its posterior part, reinforced by the attachment of the pedicles, and supported by the sturdy vertebral arch, seldom gives way. It must be noted that although hyper-flexion readily takes place, the strong anterior longitudinal ligament prevents hyper-extension. In consequence, there is a great preponderance of fractures due to flexion, whilst those due to extension are rare. The normal postural curves of the spine also make hyper-flexion common when vertical compression takes place.

Flexion fractures

Mechanism.—(1) The patient falls from a height in the standing or sitting position, or is standing in a down-going cage which is violently arrested.

(2) A heavy weight falls on the shoulders or upper dorsal region. The compression fractures, not uncommon in mining, are usually caused by this means.

(3) A blow on the back from a falling weight or from a motor vehicle, if of sufficient intensity, not only flexes the spine but adds a traversing momentum causing fracture-dislocation (Jones, 1940).

(4) Fracture of the body of a vertebra can be caused by violent muscular action alone: Palmer (1939) and Blair (1940) report cases of compression fracture of the mid-thoracic vertebral bodies occurring as the result of convulsions artificially produced in the treatment of psychiatric disorders. In some of the cases of compression fracture described in this paper, the contusion from the fall of stone which caused the injury was seen on the back directly over

the injured vertebra. It is probable that, in some of these fractures, the mechanism is not a passive hyper-flexion but an active flexion resulting from a violent contraction of the flexor muscles, perhaps a reflex protective mechanism from the blow on the back.

One or more bodies are compressed in varying degree. The simplest type of vertebral-body flexion-fracture is that in which the anterior upper edge is broken off (marginal fracture). In view of the fact that these fractures are caused by flexion, they have been grouped with the compression fractures in this series of cases. The great majority of the compression fractures occurred in the dorso-lumbar region (figure 1), the commonest fractured bodies being the eleventh and twelfth dorsal and the first and second lumbar.

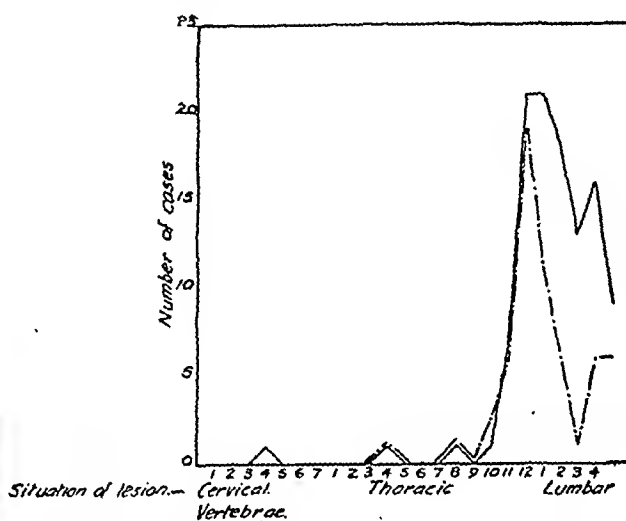


Fig. 1.—Continuous line: The site of injury in fifty cases of vertebral fracture or dislocation.

Dotted line: The site of injury in forty cases of compression fracture.

(In those cases in which more than one vertebra is involved, each fracture is marked separately.)

A distinction is drawn by Platt (*loc. cit.*) and Jones (1940) between simple wedge compression-fractures caused by the mechanism of vertical compression, when several bodies are usually compressed, and wedge compression with comminution caused by the mechanism of flexion, when usually only one body is fractured. This latter type is said to be common in miners. In the cases under consideration, the majority were due to a fall of stone on the back, but only 26 per cent showed comminution. On the other hand, two cases caused by vertical compression (sudden arrest of a down-going cage) had comminuted fractures. It appears that either type of fracture may result from either mechanism. The distinction between the two types is said to be important, since the vertebral disc is usually ruptured when comminution is present, and union is slower.

Fractures occurring through flexion show a forward dislocation of the upper segment of the spine if the violence is of sufficient severity.

Jones (1938), reviewing 252 cases of vertebral-body fracture, found that 27 per cent had a fracture-dislocation. The injury consisted of :—

(1) A compression fracture of the body of a vertebra.

(2) (a) A dislocation of the articular processes, or (b) fracture of the articular processes, or (c) fracture of the pedicles.

Cases of wedge fracture often show more compression on one side than the other.

Extension fractures

For the reasons previously given, these fractures are rare; apart from case 27 which may have been caused by extension, none is included in the author's cases. In one type, a T-shaped fracture of the anterior half of the vertebral body occurs, the anterior longitudinal ligament and inter-vertebral disc remaining intact. In another, the pedicles may be fractured. Traumatic spondylolisthesis has also been described, produced suddenly by a severe injury and associated with sacral nerve injury. Hyper-extension of the head may cause fracture of the posterior arch of the atlas.

Fractures of the muscular processes

1. *Transverse processes.*—Fractures of these processes are common in the lumbar region. The mechanism of the injury is stated by Böhler (1935) to be a sudden unguarded contraction of the quadratus lumborum, or a violent contraction of this muscle in preventing movements of the spine to the opposite side after an accident. It has been suggested by Hall and Morley (1940) that severe lumbar contusion is the most frequent cause of fracture of the transverse processes. In case 11 there was a history of a direct blow, but the other cases of this type described here were due to falls of stone on the back, site unrecorded. Of the sixteen cases of Hall and Morley, eleven gave a history of a blow in the lumbar region, whilst in five the history was indefinite.

The fracture of one transverse process is rightly not considered serious, but when several on the same side are fractured, there is an associated extensive tearing of aponeurosis, muscles, tendons and nerves. There is usually wide separation of the fragments, and union does not take place. In cases 3, 12 and 29 in which fractures of several transverse processes occurred, the patients ultimately became permanently partly disabled, but two of these patients had other injuries in addition.

2. *Spinous processes.*—These may be broken by a direct blow or by muscular violence. The fractures of spinous processes included in this series all appear to have been caused by muscular or ligamentous strain involved in hyper-flexion, or perhaps in case 27 in hyper-extension, and were associated with other severe fractures of the spine. No cases of 'shoveller's disease' have been seen. This is a fracture of the spinous process of the first dorsal or seventh cervical vertebra, which occurs as a result of muscular

violence when shovelling. This type of fracture has been described by Debueh and Matthes (1937) as occurring frequently in Germany.

Fractures of the pedicles, articular processes and laminae

Fractures of the articular processes are not uncommon in the dorso-lumbar flexion-fracture-dislocation caused by the third mechanism mentioned above; less commonly the pedicles may be fractured in association with this injury. Cases have been recorded of the pedicles alone being fractured by hyper-extension. Severe injuries accompanied by rotational and shearing forces result in fractures of articular processes, pedicles or laminae. Bilateral fracture of either the anterior or posterior arch of the atlas is caused by vertical compression such as a blow, or a fall on the head. The posterior arch may also be fractured by forcible hyper-extension of the head. When compression is present in addition, the odontoid process of the axis may break, or fracture of the posterior arches of both the atlas and axis may result. Forward flexion of the head may dislocate the axis forward. If this is combined with a fracture of the odontoid process, to which the atlas is firmly held by the transverse ligament, the spinal cord may escape damage, but if the ligament is torn and the odontoid process remains intact, death is likely to be instantaneous.

Dislocations

The commonest is the dorso-lumbar subluxation caused by hyper-flexion, in which a compression fracture of a body is associated with a fracture or dislocation of the articular processes. There is usually a forward subluxation of the upper segment of the spine, but cases occur in which the lower segment is displaced forwards. Another interesting condition is that illustrated by cases 4, 9 and 22, in which the compressed vertebra is slightly subluxated posteriorly in relation to the segments both above and below. Platt (*loc. cit.*) mentions that the association of a compression fracture with dislocation is also common in the lower cervical region. Rotation combined with flexion, or flexion alone, produces unilateral or bilateral dislocation of the cervical vertebrae, with or without fracture.

Trauma to the inter-vertebral disc

Although the disc is frequently affected in vertebral fractures, it is striking how much damage occurs to the bone with but little to the disc. Lesions which may occur are :—

(a) Fracture of the cartilage plates with hernia of the nucleus pulposus.

(b) Spongiosa collapse without fracture of cartilage plates but with expansion of the nucleus.

(c) Damage to the annulus in its posterior part with herniation of the nucleus into the spinal canal.

(d) Fracture of the anterior upper edge of the vertebra (marginal fracture of the body) involving the cartilage plate, may result in loss

TABLE I
The type, mechanism and site of injury

Case number	Injury	Mechanism	Site	Case number	Injury	Mechanism	Site	Case number	Injury	Mechanism	Site
1	C. C.	F/S.	D. 12	19	C.	F/60	D. 4	35	T.	F/S.	Lc. 1, 2,
2	C.	F/iron	D. 11, 12	20	* Di. In.	B/head	Ce. 4				3, 4.
			L. 1	21	C. T.	F/S.	D. 11, 12	36	C. T.	F/S.	D. 12
3	T.	B/sacrum	R. 1, 2,				L. 1				L. 1, 2
			3, 4.	22	C. C. S.	F/S.	L. 2	37	T.	F/S.	R. 2, 3, 4
4	C. S. P.,	F/20	L. 1, 2,	23	C. C.	F/ladder	L. 1	38	* C. C. X.	F/20	L. 1, 4
	La. Sp.		3, 4, 5.	24	C. C.	F/S.	D. 12		La. P.		
	T.			25	C. C.	F/S.	D. 12	39	C. C.	F/S.	L. 2
5	C. T.	F/S.	L. 3, 4, 5	26	C.	A/C.	D. 8	40	C. C.	F/S.	L. 4
6	C. C.	F/S.	D. 12	27	* Di. Sp.	F/S.	L. 2, 3,	41	C.	F/S.	D. 11, 12
7	C. T.	F/S.	L. 1, 2		A. T.		4, 5.	42	C. C.	F/S.	D. 10
8	C.	F/S.	D. 12	28	C. P. La.	F/6	D. 12	43	M.	F/S.	L. 4, 5
9	C. S.	F/S.	L. 1	29	T.	F/S.	Le. 1, 2,	44	C.	F/S.	L. 1
10	* C.	F/S.	D. ?				3, 4, 5.	45	C.	F/S.	D. 11
11	M. T.	B/lumbar	L. 2, 4, 5	30	C. C.	A/C.	D. 12	46	M. T.	F/S.	L. 2, 3, 4
12	T.	F/S.	R. 1, 2, 3		& C.		L. 1	47	C.	F/S.	L. 1
13	C.	F/steps	L. 1	31	C. T.	F/S.	D. 12	48	C.	B/shoulders	D. 12
14	T.	F/S.	R. 4				L. 1				L. 1
15	M.	B/lumbar	L. 3, 4, 5	32	C.	F/S.	?	49	T.	F/S.	R. 2
16	M. C.	F/10	D. 11, 12	33	C. M.	F/ladder	D. 11, 12	50	C. T.	F/S.	L. 2, 3, 5
17	C.	F/S.	D. 12				L. 1				
18	C.	F/50	L. 5	34	C.	F/S.	L. 1, 2				

Key to abbreviations in Table I

A/C. = Sudden arrest of down-going cage.
A. = Fracture of articular processes.
B/sacrum = Direct blow on sacrum.
C. = Compression fracture of vertebral body.
C. C. = Compressed comminuted fracture of vertebral body.
Ce. = Cervical.
D. = Dorsal.
Di. = Dislocation.
F/S. = Fall of stone.
F/20 = Fall of 20 feet.
In. = Interlocking of articular processes.

L. = Lumbar.
La. = Fracture of laminae.
Le. = Left.
M. = Marginal fracture of vertebral body.
P. = Fracture of pedicles.
R. = Right.
S. = Subluxation.
Sp. = Fracture of spinous processes.
T. = Fracture of transverse processes.
X. = Displacement of posterior part of vertebral body compressing cauda equina.
* = Cases in which paraplegia was present.

of substance of the disc and later degenerative change and collapse.

(e) After subluxation, the disc may be injured or deformed, and undergo degeneration.

Saunders and Inman (1939) say that, in animals, healing of wounds of the annulus is poor, and gaps may persist for several months. In most cases the disc collapses, and limitation of movement results (plate IX, figure 17).

Spinal cord injury

In the present series, only four cases showed this complication, but amongst two hundred consecutive cases of fracture of the spine described by Wortis and Sharp (1941) there were neurological complications in 73 per cent of cervical injuries, of which 75 per cent died; in 58 per cent of thoracic lesions, of which 52 per cent died; and in 24 per cent of lumbar cases, of which 4 per cent died.

Some degree of recovery of function is the rule in cases which survive, since the cord is more commonly bruised or compressed than actually lacerated or transected. The usual pathological change in a cord lesion is hæmorrhage into the grey matter. On admission, the patient is in a state of spinal shock; paraplegia and sensory

loss are at their maximum. It is impossible at this stage to be sure of the nature of the injury to the cord, or to foretell how far recovery is probable. Unless the cord is transected, some degree of recovery is seen within a few days. If there is no sign of improvement within a fortnight, it is unlikely that any will occur. In minor cases of cord damage, paralysis may be present in muscles innervated from a higher level than that at which sensory loss is present.

The prognosis is good in cases with little or no sensory loss.

Three of the four cases of cord injury described here died, and the fourth recovered only sufficiently to be able to walk with crutches. It is accepted that this complication makes a fracture of the spine a particularly grave injury.

Diagnosis

(1) When there is a history of a fall from a height, or of a blow on the back, fracture of the spine must be considered. Unless this is borne in mind, cases with minor degrees of compression may pass unobserved.

(2) Pain is a prominent symptom. In spite of this, it is still possible to overlook the presence of a fracture, since there are usually severe

contusions and abrasions to which the pain may be attributed. Jones (1940) points out that fractures in the upper and middle thoracic region are associated with much milder symptoms than those in the cervical, lower thoracic or lumbar vertebrae. Some of the cases of compression fracture in the thoracic region, caused by convulsion therapy and recorded by Blair (*loc. cit.*), made no complaint of backache or other symptoms. A series was examined radiologically to determine the incidence of spinal fracture in artificially produced fits. The author has recently treated a case of compression fracture of the eighth dorsal vertebra (not included in this series) in which no pain whatever occurred at the site of compression before or after reduction. The degree of compression was slight, and complete reduction was obtained by the operating-table kidney-bridge method.

Nevertheless in compression fractures, the pain is usually severe and diffuse, and radiates to both sides. It is maximal at the injured vertebra, and is felt both above and below that level. Active movements are usually avoided, but some patients with compression fracture are able to walk. Passive movements are accompanied by muscular spasm and pain, but this is usually not of sufficient severity to prevent reduction by hyper-extension without anaesthesia. The spinous process of the affected vertebra is remarkably tender, and this tenderness is also diffuse, being present over several vertebrae above and below the fracture, and over the adjacent sacrospinalis. It is probable that this tenderness and much of the pain are due to the tearing of the supraspinous and interspinous ligaments concomitant with a traumatic kyphosis.

When transverse processes are fractured, the pain is again severe and diffuse, often leading to a suspicion of compression fracture, but maximal tenderness is felt over the injured bone. Since the diagnosis can be made with certainty only by radiological examination, a prolonged physical examination of a case of fracture of the spine is best avoided, as the pain thus inflicted may increase shock.

(3) A tender swelling is present in the back in cases of compression fracture. This is partly due to the traumatic kyphosis, and partly to the soft tissue-swelling and local effusion of blood which accompanies any fracture. It is probable that, like the tenderness and pain, much of this swelling is caused by rupture of the supraspinous and interspinous ligaments. An important diagnostic point is the prominence of one spinous process.

(4) If paralysis and anaesthesia are present below the site of the injury, the diagnosis is practically certain, but radiological examination is still essential in order to ascertain the type of fracture or dislocation present.

(5) A good lateral skiagram is necessary in addition to one in the antero-posterior plane, as the latter does not reveal what degree or kind of fracture is present, or whether subluxation has occurred.

A practical point arises in connection with taking of the lateral skiagram. It is known that extension of the spine without anaesthesia corrects the deformity, and that flexion accentuates it. It therefore appears likely that, at any rate in some cases, the position of the patient during radiological examination influences the apparent degree of compression. Although flexion of the spine before taking the skiagram is not advocated, as this might complicate the fracture, yet it seems advisable to stress the importance of taking the lateral view in the neutral rather than in an over-extended position, in order to facilitate a true conclusion as to the severity of the injury. This point is said to be of particular importance when dealing with suspected minor degrees of cervical subluxation.

Treatment

(1) *First aid.*—In all cases of fracture of the vertebrae, whether of the body, processes, laminae or pedicles, movements of the spine must be reduced to a minimum. In addition it is clear that flexion, whereby the majority of the fractures are caused, must be entirely avoided, as it may accentuate the degree of compression and may even damage the spinal cord. These points are very properly referred to in first-aid books, where the need for carefully turning and transport is stressed; since compression fractures are reduced by hyper-extension, and since the sacrospinalis is relaxed in this position, and the pain in fractures of the muscular processes is thereby diminished. Hyman (1939) has recommended that special convex stretchers should be used for these cases, the patient lying supine. The main use of such a stretcher would lie in transport in hospital from the x-ray room and to and from plaster rooms. Its use is contra-indicated before the skiagrams have been examined, for in the uncommon hyper-extension fractures, harm might result. Cases of fracture-dislocation with interlocking of articular processes would suffer severe pain on such a stretcher.

The first-aider should aim at preserving the neutral position. If the patient is lying face downwards, he should be lifted in that position by any of the special first-aid methods, and placed on a stretcher with a support under the shoulders and groins. If lying on the back, the patient may be turned on to the face or lifted as he is, with the addition of a special support under the dorso-lumbar region, to prevent flexion. This support is retained when the patient is on the stretcher. When the patient is unconscious, or the injury is in the region of the neck, he is lifted and transported supine, and the head is supported in the neutral or extended position. The first-aider must treat shock, but if a spinal cord injury is present, careful lifting is even more important.

(2) *Orthopaedic treatment.* (a) *Cases without paraplegia.*—The method of treatment and, in

consequence, the prognosis, have changed fundamentally in the last few years. Until 1929 it was the custom, if the diagnosis was made, to treat the patient in a plaster bed and, when consolidation

by infiltration between the spinous processes as advocated by Böhler (*loc. cit.*) appears unnecessary, as excellent reductions are obtained without it.

TABLE II
Summary of initial and final degrees of compression and method of reduction

Case number	DEGREE OF COMPRESSION		Method of reduction	Case number	DEGREE OF COMPRESSION		Method of reduction
	Initial	Final			Initial	Final	
1	50%	Slight	D.	25	50%	Slight	D.
2*	Slight, 25%, 30%	Nil	D.	26	50%	50%	W.J.
4	20%	Nil	D.	28	40%	15%	W.J.
5*	20%, slight	?	D.	30*	50%, 10%	Nil, 10%	W.J.
6	30%	15%	D.	31*	50%, slight	?	W.J.
7	20%	Nil	D.	32	Skiagram not available.		W.J.
8	40%	15%	D.	33	Slight	Nil	W.J.
9	70%	70%	D.	34*	10%, 10%	10%, 10%	W.J.
10	No skiagram		D.	36	Slight	Nil	W.J.
13	30%	10%	D.	38	50%	Slight	D.
16	Slight	Slight	D.	39	30%	Slight	W.J.
17	20%	?	D.	40	Unknown	Nil	W.J.
18	40%	40%	D.	41*	20%, 20%	Nil	W.J.
19	10%	10%	D.	42	20%	Nil	W.J.
21	Slight	Slight	D.	44	Unknown	Nil	W.J.
22	60%	50%	D.	45	Slight	Slight	W.J.
23	25%	Nil	D.	47	25%	25%	W.J.
24	60%	30%	D.	48	Slight	Nil	W.J.
				50	Slight	Slight	W.J.

Methods of reduction

* Multiple lesions.

D.=Reduction by Davis' method under general anaesthesia followed by application of plaster-jacket.

Case 23 was reduced by this method without anaesthesia.

W.J.=Reduction by Watson-Jones two-table method followed by application of a plaster jacket.

had occurred, to allow walking. Intractable pain was a common sequel, and this was met by a spinal fusion or the wearing of a brace. There was much argument whether laminectomy should be performed or not in cases complicated by spinal cord injury. In 1929 Davis published an important paper giving details of a method of reduction of compression fractures by hyper-extension and manipulation under anaesthesia. He recognized that wedge fractures are due to hyper-flexion, and reduced them by hyper-extension under anaesthesia, by pressure over the kyphosis, and by the application of a plaster bed. Hyper-extension was effected by placing the patient in the prone position and hoisting the heels vertically until only the upper part of the trunk and head of the patient remained in contact with the table. A further advance in treatment was the 'two table' method of reduction described by Jones (1931). The upper parts of the patient's thighs rest on a low table, whilst the arms are supported on a higher one, the trunk sagging, with extension of the spine, between the two supports. No anaesthetic is administered and no manipulation performed. By both these methods the spine becomes completely extended to the limits of the anterior longitudinal ligament. In the first method, however, the degree of hyper-extension depends on the depth of anaesthesia, and in the second method on the patient's co-operation and ability to relax. Local anaesthesia

The author has not been successful in attaining complete reduction by using the Davis technique, except in case 23 in which no anaesthetic was administered. It may be that this lack of success was due to the depth of anaesthesia being insufficient to allow enough muscular relaxation. In contrast, the degree of reduction obtained by the Watson-Jones technique has been gratifying, and it is concluded that, in reducing compression fractures of the vertebral body, the two-table method without anaesthesia is the better. If other considerations make the administration of an anaesthetic imperative, this procedure is impracticable, and the Davis method is employed. The use of a motor-car jack or the kidney-bridge of an operating table in reduction has been described. The latter method is useful in high dorsal fractures which are difficult to reduce by other means.

In applying a plaster jacket, about ten plaster bandages, twelve inches wide by eighteen feet long, are needed. When a dorso-lumbar fracture is present, the plaster reaches from the manubrium sterni to the pubes, and, in high dorsal and cervical fractures, the neck and shoulders must be included. A quarter of a grain of morphia is administered by hypodermic injection half an hour before reduction. The patient is given a sense of security by an assistant grasping the ankles lightly. By raising them gently he

may be able to assist the patient's efforts at hyper-extension. Two more assistants hold the patient's forearms in order to prevent them slipping off the table. For comfort, a pad is placed between each arm and the edge of the table, and the upper parts of the thighs rest on a pillow on the edge of the lower table. During application, the patient is instructed to breathe deeply, thereby obtaining a little extra room in the plaster. Pressure sores are apt to occur in the upper lumbar region, and a pad of cotton-wool is placed there to prevent them. Partial turning of the patient every few minutes during the first forty-eight hours is the most important factor in the prevention of pressure sores. When the plaster has been applied, a lateral skiagram is taken to ascertain if the reduction is satisfactory. An epigastric window is not cut unless it is essential as a result of distension. The patient is allowed to walk as soon as the plaster is quite dry, provided that there are no complications, and he attends as an out-patient for the greater part of his period of treatment. Exercises for the abdominal and spinal muscles are practised from the first. These consist in flexing and extending the hips with the knees straight, in both the supine and prone positions. After three to four months, the patient is readmitted to hospital, the plaster is removed, further skiagrams are taken and, if these are satisfactory, walking without plaster is commenced. There is usually some pain in the back over the site of the fracture for a variable period after the plaster is removed. A slight increase in compression often takes place in the first few weeks of treatment, when the patient is ambulant (plate X, figures 18, 19 and 20). This may be ignored.

(b) *Cases with paraplegia.*—The surgeon has two alternatives: firstly, he may reduce the fracture as soon as the patient's general condition is good enough, apply a plaster, and trust to good nursing to avoid bed sores. If this course is taken, a plaster bed and turning case is better than a plaster jacket, although more arduous to make. Secondly, he may postpone reduction and the application of plaster in an effort to avoid pressure sores. The first alternative is undoubtedly preferable since, if the fracture is reduced early, there is a better chance of spinal cord recovery, and in consequence a diminution of the risk of sores.

Nursing.—Slight changes in the patient's posture must constantly be made. A useful method of relieving pressure is frequent gentle stroking of the skin where it is in contact with bed or plaster. The patient must be washed several times a day, and the skin where accessible must be rubbed with spirit and powdered in the usual way. It is particularly important to cleanse the patient immediately there is any soiling by excreta. All joints in paralysed limbs should be gently put through full passive movements daily.

The bladder.—In the early stage of retention of urine, the tying in of a catheter is a satisfactory method of treatment. The catheter should be changed at intervals of a week. Later, patients with retention and overflow should have a suprapubic cystostomy performed, and should have daily bladder irrigations.

Fractures of single transverse processes without much displacement are treated by three to four weeks' recumbency followed by massage and exercises. Even though union often does not occur, there is no permanent disability. When several transverse processes on one side are fractured with separation, there is extensive tearing of soft tissues, and treatment in a plaster jacket with some degree of extension to relax the muscles is advisable for from two to four months.

(3) *Open reduction.*—In dorso-lumbar fracture-dislocations, the upper vertebral body is usually displaced anteriorly in relation to the lower one. If the articular processes are fractured, reduction may be obtained by manipulation, but if they are not, an insuperable obstacle to reduction is formed by the impinging of the posterior surface of the inferior articular process on the anterior surface of the superior articular process. This interlocking may take place on one or both sides. Immediate operation is called for; the processes are exposed and the tips of the superior articular processes are removed until reduction can be obtained by manipulation before closing the wound. Adams (1938) and Munro (1938) describe successful reduction performed in this way.

If there is conclusive evidence of the presence of bone fragments in the neural canal, and an incomplete cord lesion is present, laminectomy should be performed. This operation is also indicated when an incomplete cord lesion progresses in severity, provided that lumbar puncture below the injured level reveals a blockage in the spinal canal. Laminectomy should never be performed in the presence of a complete cord lesion. Wortis and Sharp (*loc. cit.*) describe a series of fifteen laminectomies in two hundred spinal fractures. Eight of the fifteen patients died, five were not improved and two showed improvement.

Dislocation of the cervical vertebrae

Unilateral or bilateral dislocation of the cervical articular processes can be reduced by strong traction on the head combined with manipulation (case 20). The extension is applied skeletally by means of special calipers in small trephine holes in the skull, or by a sling under the chin and occiput. The reduction is followed radiologically whilst the traction is gradually increased. In case 20, when a weight of 70 lb. was reached, the articular processes became disengaged and by anterior pressure on the upper cervical spine, and posterior pressure on the lower cervical spine, reduction was effected and the weight gradually lessened (plate IX, figures 6 and 7). After reduction, a well-padded plaster

collar including the upper chest is applied. Minor degrees of subluxation without dislocation of the articular process may occur from trivial violence, for instance, in a passenger in a suddenly braked car. In these cases, the lateral skiagram must be taken in the flexed position, otherwise spontaneous reduction may occur con-

pain due chiefly to the strain on the inter-articular joints, but the degree of pain lessens for about two years after the injury.

Cases with multiple vertebral fractures are naturally more serious than those with simpler injuries. In those with symptoms of spinal cord compression, the prognosis is bad.

TABLE III
End results

Case number	Result	REMARKS	Case number	Result	REMARKS
1	30% C.	Subluxation not reduced.	27	D. 16th day	Fracture of ribs and skull.
2	30% C.		28	W.	
3	20% C.		29	30% C.	
4	30% C.		30	W.	
5	20% C.		31	20% C.	
6	W.		32	L. W.	
7	W.	Probably an old compression fracture unrelated to the recent injury. Complicated by cut ligamentum patellæ.	33	W.	Compound fracture 5th left metatarsal.
8	25% C.		34	W.	
9	Defaulted		35	W.	
10	D. 1st day		36	W.	
11	W.		37	W.	
12	20% C.		38	100% C.	
13	W.	Became insane. First seen one month after injury.	39	W.	Initially complete paraplegia below D. 12. Finally below L. 4.
14	W.		40	W.	
15	W.		41	W.	
16	75% C.		42	W.	
17	35% C.		43	W.	
18	15% C.	First seen two months after injury.	44	50% C.	Fracture of ribs, humerus and nose.
19	15% C.		45	W.	
20	D. 3rd day		46	W.	
21	W.		47	15% C.	
22	30% C.		48	W.	
23	W.		49	20% C.	
24	30% C.	Fracture of both calcanei and right talus.	50	W.	Fracture of R. 5th metatarsal. Fracture of right 5th metatarsal.
25	20% C.				
26	70% C.				

C. = Compensation awarded.
W. = Returned to work.

D. = Died.
L. W. = Light work.

cealing the true nature of the injury. Treatment is by plaster immobilization in full extension for three to four months.

When fracture of the articular processes accompanies a cervical dislocation, treatment must be by continuous traction. Fracture of the atlas is treated by plaster in mid-position if there is no paraplegia, and by continuous traction if there is paraplegia. Forward dislocations of the atlas are treated by plaster splintage in extension.

Prognosis

This depends on the severity of the fracture and the degree of reduction obtained. In fractures of one or two transverse processes without much displacement, it is good. Those patients with fractures of several transverse processes with wide separation may have prolonged pain.

Patients with moderate degrees of compression of vertebræ, well reduced and adequately treated, return to work within six or seven months. Those not well reduced generally cause permanent

Discussion

Some details of fifty consecutive cases of fracture and dislocation of the spine occurring in miners on the Kolar Gold Field are given in the tables I, II and III above.

Table IV summarizes the types of injury met with.

The results of treatment in the various groups are given in table V.

Percentages are given as well as actual figures, although it is realized that with such small numbers statistical conclusions may be erroneous.

Only one cervical dislocation was met with. Cases of fracture of the spine recorded by other authors reveal a heavy incidence in the lower cervical region. In a statistical study of 2,006 cases collected from various sources, Jefferson (1928) found the heaviest incidence at the level of the sixth cervical vertebra, the next heaviest at the first lumbar and the next at the second cervical. This study took place before surgeons were familiar with the mild degrees of dorso-lumbar compression.

TABLE IV

Details of trauma in fifty consecutive cases of fracture and dislocation of the spine

Group	Nature of fracture	Number of cases	Percentage of total
1	Simple compression fracture of vertebral body (including fractures of anterior upper edges of bodies) without other spinal injury.	19	38
2	Compression fracture of vertebral body with comminution	9	18
3	Compression fracture of vertebral body with fracture of transverse processes.	8	16
4	Fracture of transverse processes without other spinal injury	7	14
5	Compression fracture of vertebral body with subluxation	1	2
6	Compressed comminuted fracture of vertebral body with subluxation ..	1	2
7	Compression fracture of vertebral body with transverse fracture of pedicles and laminae.	1	2
8	Compression fracture with collapse of posterior part of body narrowing spinal canal and transverse fracture of pedicles and laminae at another level.	1	2
9	Compression fracture of vertebral body with subluxation, fracture of articular, spinous and transverse processes, and transverse fracture of pedicles and laminae.	1	2
10	Fracture-dislocation of vertebral body with fracture of articular, spinous and transverse processes.	1	2
11	Cervical dislocation	1	2
		50	..

TABLE V

Results of treatment—the groups are those classified in table IV

Group	RETURNED TO WORK		COMPENSATED FOR PERMANENT PARTIAL DISABILITY		DIED	
	Number of cases	Percentage of total	Number of cases	Percentage of total	Number of cases	Percentage of total
1	10	53	8	42	1	5
2	7	78	2	22
3	6	75	2	25
4	3	43	4	57
5
6	1
7	1
8	1
9	1
10	1	..
11	1	..
TOTAL	27	54	19	38	3	6

Wortis and Sharp (*loc. cit.*), in their two hundred consecutive cases, found the incidence highest in the dorso-lumbar reign; fifty cases involved the first lumbar vertebra, but cervical injuries were also frequent, twenty cases affecting the sixth, and ten the second cervical vertebra. The majority of their cases were caused by falls from a height, or by automobile accidents. In the cervical region, the commonest

injury was a fracture-dislocation, in the thoracic region, both fracture-dislocation and compression fracture occurred, and in the lumbar region the vast majority were compression fractures.

It appears that fractures of the spine occurring in miners are predominantly dorso-lumbar.

Most of the author's patients who returned to work continued their previous occupations as labourers (a strict criterion of recovery), but

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a few were given light employment temporarily. Those who received compensation mostly received small percentages for persistent pain. If there seemed no likelihood of a patient returning to work after several months' treatment, he was offered compensation for permanent partial disablement. It is noteworthy, however, that after satisfactory treatment, pain is likely progressively to diminish over a period of eighteen months to two years, and that it is only after this time that the final result can be properly assessed.

Of seven patients with fracture of the lumbar transverse processes without other vertebral injury, three returned to work and four received compensation. The severity of this injury is

to work, eight (42 per cent) received compensation and one (5 per cent) died. It is noteworthy that these results are inferior to those in which there was in addition either fracture of the transverse processes or comminution.

In view of the fact that group 1 of simple compression-fractures includes several comparatively mild injuries—those with marginal fracture of the body—the number of patients who returned to work, although good, is not as high as might be expected. The reason for this becomes clear on dividing the cases into two groups according to the method of reduction.

It is seen that the Watson-Jones method of reduction has given vastly better results than

TABLE VI
Results of different methods of treatment in group 1

Method of reduction	Total number of cases	RETURNED TO WORK		COMPENSATION PAID		DIED	
		Number of cases	Percentage of total	Number of cases	Percentage of total	Number	Percentage
Davis	10	3	30	6	60	1	10
Watson-Jones ..	9	7	78	2	22
TOTAL ..	19	10	53	8	42	1	5

somewhat exaggerated by these figures, since of the four cases who received compensation, one had in addition a cut ligamentum patellæ, another had fractures of the eleventh and twelfth ribs, probable fracture of the skull, and multiple wounds, and a third had multiple wounds and other fractures. It is probably unusual for fractures of the transverse process alone to lead to permanent pain and disablement. This is borne out by the results in group 3 (tables IV and V) of cases of compression-fracture with fracture of transverse process. Of these eight cases, six returned to work and two received compensation, these facts suggesting that the additional fracture of the transverse processes did not materially alter the prognosis.

Groups 1, 2 and 3, the cases of simple compression, compression with comminution, and compression with fracture of transverse processes, constitute a series of thirty-six compression-fractures without serious additional vertebral injury. They form 72 per cent of the total cases of spinal injury described. Twenty-three (64 per cent) of these returned to work, twelve (33 per cent) received compensation, and one (3 per cent) died.

The results in cases with comminution (group 2) were considerably better than in those without. It does not appear, therefore, from this series, that the presence of comminution indicates a fracture of exceptional severity or a bad outlook.

Amongst the nineteen simple compression-fractures in group 1, ten (53 per cent) returned

to work. The failure of the latter procedure may be attributed to:—

(1) Deficient muscular relaxation under anaesthesia. (It will be noted that case 23 treated by the Davis method without anaesthesia was well reduced.)

(2) It may be that hyper-extension is less complete than in the Watson-Jones method where the sagging of the trunk due to the force of gravity between two tables results in a tendency for the pressure on the thighs and arms to bend the back forcibly.

The cases remaining in groups 5 to 10 all had serious complications such as dislocation, or fracture of articular processes or pedicles. Nevertheless case 28, in which there was a compression-fracture with transverse fracture of the pedicles and laminae, returned to work as labourer. Case 38 had a similar injury to the pedicles and laminae at a lower level than his compression-fracture. This lesion, seen in cases 4, 28 and 38, is an interesting one. It appears as though the fracture line passes right through the vertebral body and neural arch. Whilst the posterior part of the body remains apparently intact, the hyper-flexion causes a collapse of the anterior part of the body, and a splitting and opening of the pedicles and laminae.

Of the remaining cases in groups 5 to 10, three received compensation, one defaulted and one died.

The total number of cases of compression-fracture including the complicated cases was 41. Twenty-four (59 per cent) of these returned to

KEY TO PLATE IX

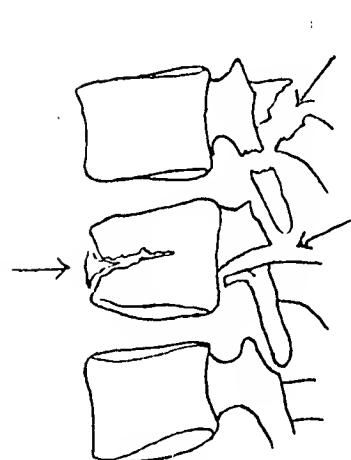


Fig. 2a.

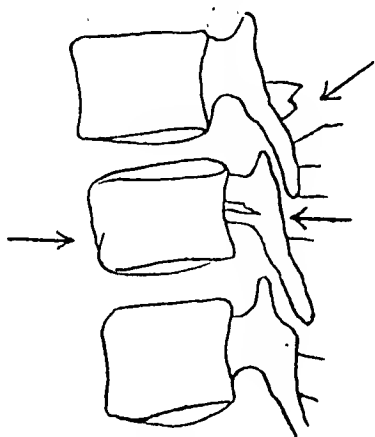


Fig. 3a.

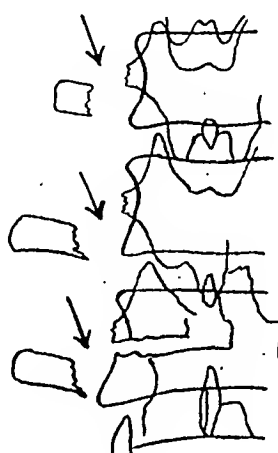


Fig. 4a.

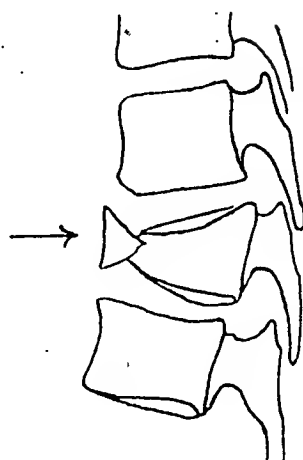


Fig. 5a.

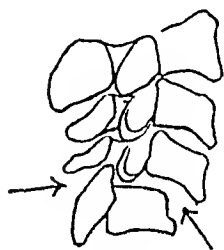


Fig. 6a.

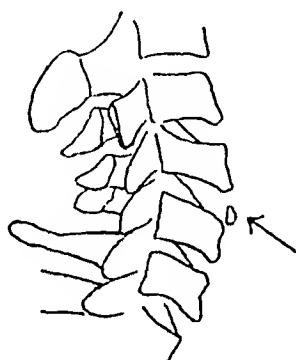


Fig. 7a.

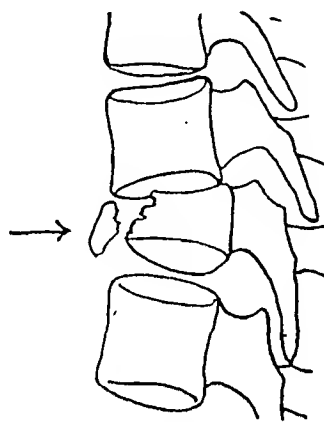


Fig. 8a.

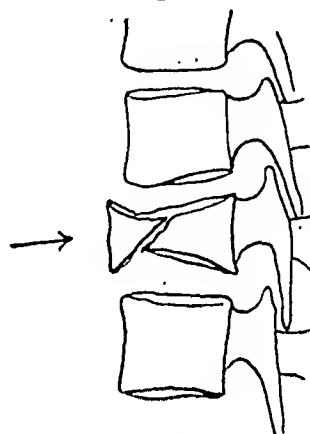


Fig. 9a.

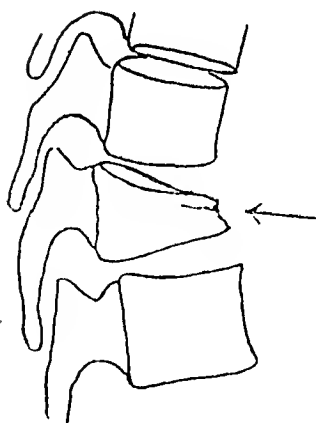


Fig. 10a.

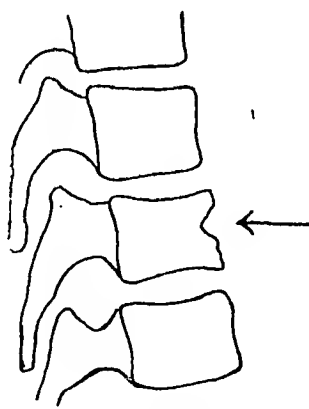


Fig. 11a.

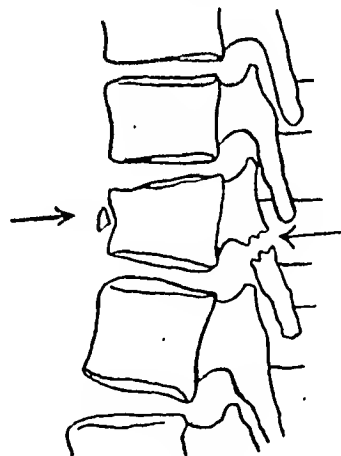


Fig. 12a.

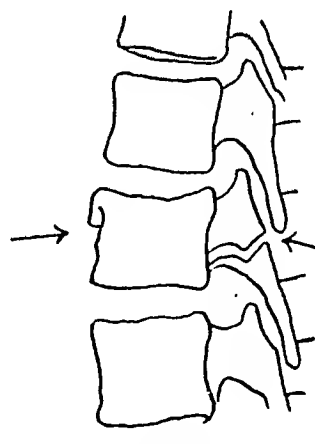


Fig. 13a.

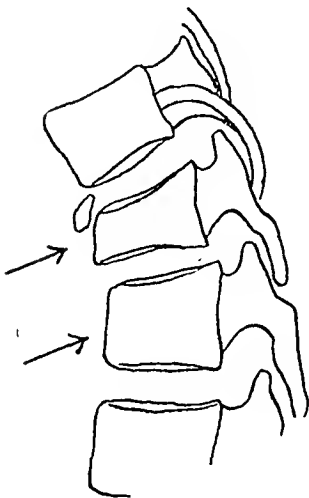


Fig. 14a.

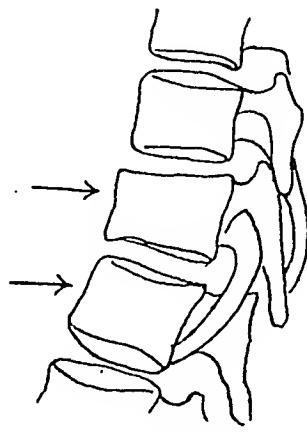


Fig. 15a.

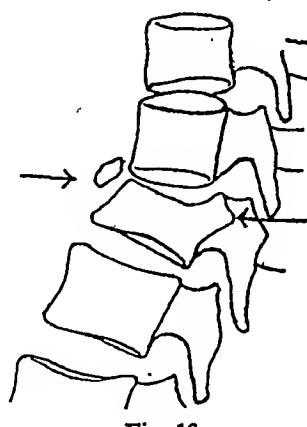


Fig. 16a.

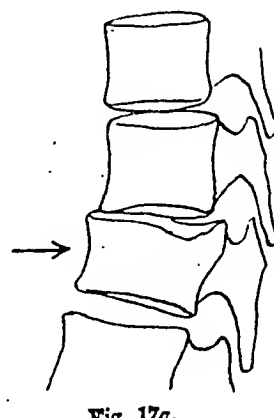


Fig. 17a.

PLATE IX
 FRACTURES AND DISLOCATIONS OF THE VERTEBRÆ : G. E. DUNKERLEY



Fig. 2.



Fig. 3.



Fig. 4.

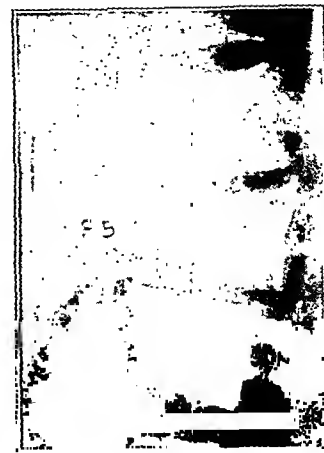


Fig. 5.



Fig. 6.



Fig. 7.



Fig. 8.



Fig. 9.



Fig. 10.



Fig. 11.



Fig. 12.



Fig. 13.



Fig. 14.

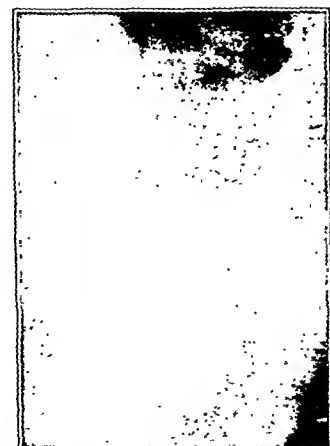


Fig. 15.



Fig. 16.



Fig. 17.

PLATE X
FRACTURES AND DISLOCATIONS OF THE VERTEBRÆ : G. E. DUNKERLEY

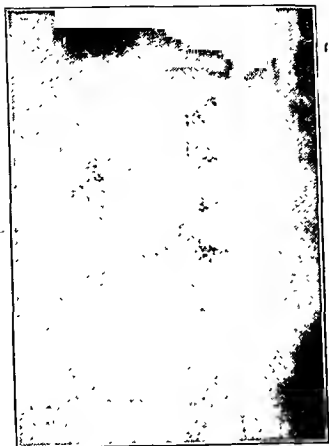


Fig. 18.

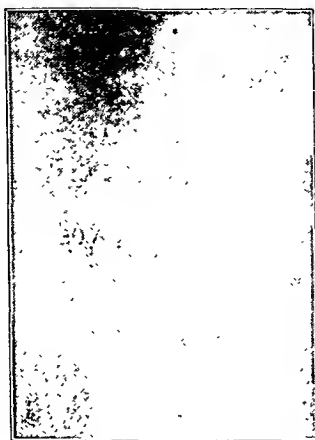


Fig. 19.

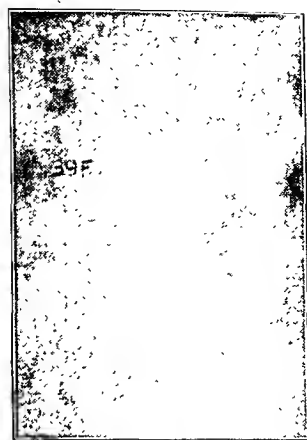


Fig. 20.

KEY TO PLATE X

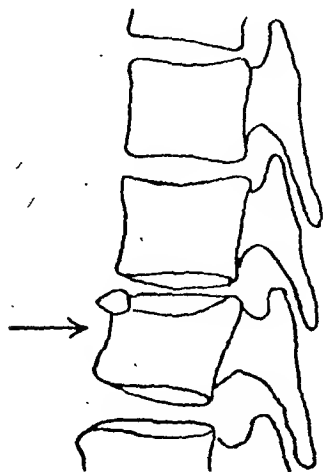


Fig. 18a.

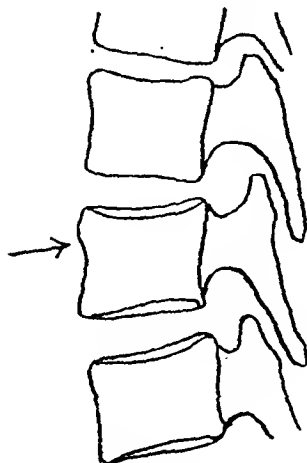


Fig. 19a.

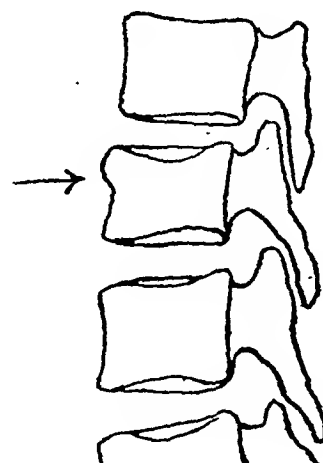


Fig. 20a.

work, fifteen (37 per cent) were paid compensation, one (2 per cent) died and one (2 per cent) defaulted.

There were four cases with spinal cord compression symptoms in the series. Three of these died, and the other was paid compensation for total permanent disablement.

Summary

Fifty consecutive cases of vertebral injury occurring in miners are described, and the results of treatment recorded. Forty-one had compression-fracture, and three of these had subluxation in addition. One case had fracture-dislocation without compression, and one a dislocation without fracture. There were seven cases with fractured transverse processes only.

The anatomy of the vertebræ and inter-vertebral discs is outlined, and account is given of the types of injury which may involve these structures.

Diagnosis and treatment are discussed at length, and mention is made of the chief prognostic points. The Watson-Jones method of reduction of compression fractures has given better results than other methods employed.

The results of treatment are assessed as successful or unsuccessful on the basis of return to heavy manual labour or of the presence of permanent disability necessitating compensation.

Acknowledgment

I have pleasure in acknowledging my indebtedness to Dr. W. B. Roantree, Chief Medical Officer, Kolar Gold Field, for his kind help in preparing this article, and my thanks are due to Messrs. John Taylor & Sons, the Managers of the Kolar Gold Field, for permission for publication.

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EXPLANATION OF PLATES IX AND X

- Fig. 2.—Case 4 before reduction. Note slight posterior subluxation and fracture of pedicle of L. 4 and fracture of inferior articular process of L. 3.
Fig. 3.—Case 4. Final result.
Fig. 4.—Case 4. Note wide separation of fractured transverse processes.
Fig. 5.—Case 9 before attempted reduction. This lesion is the result of an old compression fracture and bears no relation to the patient's recent accident. Note posterior subluxation of L. 1.
Fig. 6.—Case 20 before reduction.
Fig. 7.—Case 20 after reduction.
Fig. 8.—Case 22 before reduction. Note posterior subluxation of L. 2.
Fig. 9.—Case 22 end result. Compare with case 9, figure 5.
Fig. 10.—Case 24 before reduction.
Fig. 11.—Case 24 after reduction.
Fig. 12.—Case 28 before reduction. Note fracture of neural arch.
Fig. 13.—Case 28 after reduction.
Fig. 14.—Case 30 before reduction.
Fig. 15.—Case 30 after reduction.
Fig. 16.—Case 38 before reduction. Note backward displacement of posterior part of body of L. 1.
Fig. 17.—Case 38 after reduction.
Fig. 18.—Case 39 before reduction.
Fig. 19.—Case 39 after reduction.
Fig. 20.—Case 39 final result. Note slight recurrence of compression in comparison with figure 19.

Public Health Section

SOME IMPRESSIONS OF PUBLIC HEALTH IN INDIA*

By M. C. BALFOUR, M.D.

Regional Director in the Far East, International Health Division, Rockefeller Foundation

THE honour of your invitation to give the third lecture to the Delhi Maternity Services Co-ordinating Committee is gratefully acknowledged. It is with a strong sense of humility that I undertake the task. After only one year's acquaintance with India, I realize fully my limited knowledge of this vast sub-continent and even of the field of public health in India.

In view of the nature of your committee, it would have been appropriate for me to select a subject within the field of maternity and child welfare, but my acquaintance with the functioning of the maternity services in Delhi or of this branch of health work in India is still so limited that I cannot discuss it adequately. On the subject of co-ordination I will only pause to remark that co-ordination and co-operation are the keystones of success in public health work. They are basic conceptions in public health or medical administration. I understand that the committee has made important progress in achieving co-ordination in this area, although additional results are still desirable in spirit and practice.

I have chosen the general topic of public health, because it gives a wider scope in which to present one's impressions. To consider public health in its entirety may also serve to illustrate the need for co-ordination in maternity and child welfare services, and of these services in relation to the other aspects of public health. For my sources of information I can only claim to have had an introduction to some important parts of the country—the three Presidencies, Delhi Province, the United Provinces and Mysore State. A visit to Ceylon has given some comparative impressions. These travels have permitted me to meet officers of the civil and medical services, the workers of certain teaching and research institutions, and to see some field activities. I am gradually increasing my familiarity with the published reports on health and medical administration in India. It is also natural that my impressions are influenced by other individuals, particularly my associates of the Foundation, who have visited and worked in India. I am thinking particularly of the survey made by Miss M. E. Tennant on Nursing in India and the observations of Dr. W. P. Jacobs and Dr. J. B. Grant.

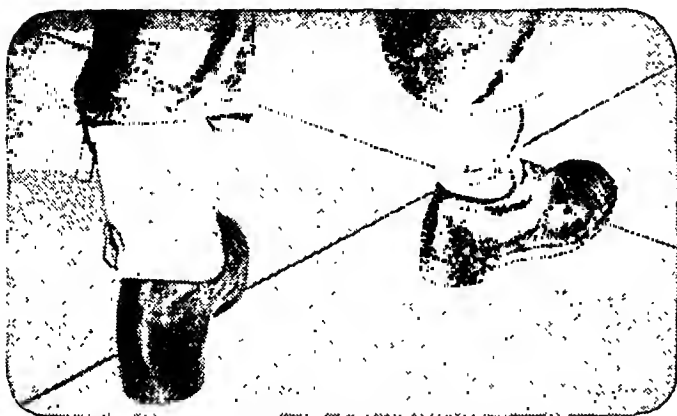
If my remarks are critical in part, it is hoped they are recognized for their intent to be constructive and friendly. In sharing the impressions with you, there is no purpose other than to fulfil in spirit the fundamental objective of our organization, which is to promote by all reasonable and productive means the welfare of mankind throughout the world. India is an increasingly important part of this world, and our health division policy is to co-operate with established governments towards that goal.

To examine the problem of public health in India, one may begin by asking, what is the state of health in India? In a manuscript by Dr. J. B. Grant on the health of India which I read recently, the first sentence begins 'The level of public health in India is low'. This concise statement is not a cheerful introduction; it may be explained but not refuted. Preventible epidemic diseases such as cholera, the dysenteries, malaria, smallpox and typhoid exact an enormous toll, as you know. The figures for British India in 1939 gave the following round number of deaths; cholera—100,000; dysenteries and diarrhoeas—260,000; malaria—1,400,000; and smallpox—50,000 deaths for the year. Even granting that some records of mortality are of questionable reliability, it is possible that they are understatements rather than exaggerated figures. I do question the records of malaria mortality in many instances, because whenever this disease is seriously prevalent, it is the scapegoat for much of the unknown and ill-defined causes of death. In comparing the death rates and infant mortality rates of India with other countries, we need only observe that these two basic rates are approximately two and three times the relative figures for England and Wales or the United States; they are definitely higher than for Ceylon and markedly higher than for Java and Japan. Statistics from other Far Eastern countries where population densities are high and economic levels are low may be examined for comparison and enlightenment, but give no comfort to India.

In the first lecture to this committee, General Jolly, the Director-General, referred to maternal mortality rates of 25 per 1,000 and said that infant mortality rates up to 35 per cent were not uncommon in India. Various surveys have given maternal mortality rates from 15 to 25 per cent. The Special Committee which reported to the Central Advisory Board in 1938 on maternity and child welfare work in India concluded that the maternal mortality rate for this country as a whole is probably somewhere near 20 per 1,000 live births, or four to five times greater than those countries where effective attention has been given to the protection of motherhood. Infant mortality figures appear to vary by years and regions from about 120 to 230, with a mean figure

* A lecture given under the auspices of the Delhi Maternity Co-ordinating Committee at New Delhi on 17th February, 1943.

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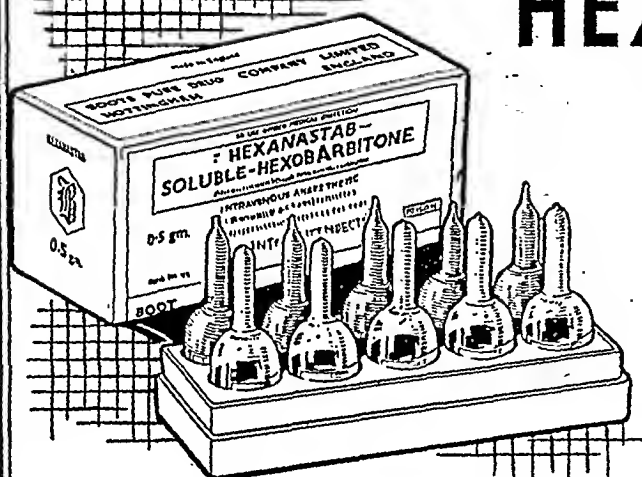
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around 160 per 1,000 births; the critical point is that the rate of decline, so well marked in other countries, is much slower in India than elsewhere.

You are undoubtedly familiar with these statistics. The only purpose in restatement is to register them as a part of my impression, and perhaps to confirm your dissatisfaction with present health conditions. I am a firm believer in the value of health discontent, or, as some may call it, divine discontent. That health workers are ever striving intelligently and sincerely for improvement, whether it is India, China, the U.S. or Great Britain, is a sign of progress and hope. Hence I trust that you will agree with the impression that public health in India is not satisfactory. There might be some consolation if we had the comparative record of India of 50 or 60 years ago, but the present figures are a formidable score for any country or region which is administered on modern lines.

The major factors which contribute to the low state of health in India are readily apparent. Among them, there is the low economic level of the population as observed in an average *per capita* purchasing power of 2½ annas daily. Secondly, the degree of illiteracy and the low educational standard are interrelated factors. Social welfare organizations, legislation and practice are still undeveloped, and those which exist affect few of the country's millions. The importance of mentioning these basic factors is to point out the need of recognizing the complex and difficult nature of the problem, and to emphasize the necessity of co-ordination in their study and solution. It is not a vicious circle which defies solution. Health and medical services should be planned and administered in conjunction with other social services. Education, agriculture, rural economics, public and social administration, and public works are each an element in the composite picture of which health and medical services form an integral part. This collaborative functioning as it affects rural populations is sometimes termed rural reconstruction. China has made progress in tackling this problem, and rural reconstruction or the co-ordination of the rural social services is a definite platform of government. India is also awake to this movement, and I believe it has been a subject of some experiments in the field. There is still need of much planning and conference among the different agencies of central and local governments for a united effort to improve and co-ordinate the social services.

In the field of medical research, India has an enviable record of accomplishment. One need only mention malaria, kala-azar, plague and cholera as the subjects of research in the epidemic and tropical diseases, to recall the outstanding contributions which British and Indian workers in this country have made. There are here numerous research institutions and associations which have a world-wide reputation. To the newcomer who knows the record of research in India, there is some disillusionment in finding

how little application of that knowledge has as yet been effected. Research or the advancement of knowledge is fundamental to the definition of the problem, and to finding the most effective and economic methods of disease control. Research which finds no outlet in the peripheral organizations and field services for bringing results to the people has not accomplished its full purpose. It is by no means suggested that less energy or support be given to research, but I question if research in India has not far outstripped the application of existing knowledge.

To face the statistical record and the public health problems of India without being disheartened, there is to my mind a need for a basic public health philosophy. A cynic may question if it is desirable and worthwhile to save lives and prevent illness in India or China. With an annual increment of three to four millions of population and not an unlimited food supply, it is a realistic question to ask, if the efforts of health and medical workers are to be logical and in accord with natural law. I fear that some of us carry on mechanically at times, doing the daily task and leaving the reasoning to others, or accepting fatalistically the conditions and results of our efforts. Before coming to the Far East, I confess I looked upon India and China as vast territories with overwhelming health problems where it might be of interest to engage in research studies, but where an amelioration of the health and medical conditions appeared somewhat hopeless. Contact with the people and their problems has brought a realization that a satisfactory health philosophy for India is not qualitatively different from the rest of the world. We must start with the premise that every individual, regardless of race, sex or religion, has a certain birthright to good health, freedom, and the pursuit of happiness or contentment. The development and progress of the individual will depend on his personal qualities, which combine the results of heredity and the effects of environment. As a further part of that credo, the individual, whether child or adult, has the right to competent health and medical care at a reasonable cost. It is conceived to be the duty of society to organize this service, if private efforts do not fulfil the needs. The expense of medical and health care, either private or public, should be in relation to the individual's or community's ability to pay for it. I have adapted this credo which is appropriate in my country to the local situation, and in its general terms I find that it is equally applicable here.

Lest a realist fear the effects of health and medical activities on population densities, it may be observed as a general truism that if death rates are reduced, the birth rate will become adjusted. Generally speaking, if the death rate is lowered, the birth rate declines, and the converse relationship is usually observed. I do not know of any country where the relationship of birth rate to death rate is not directly correlated. Whether the adjustment is biological

or purposeful, or a combination of both may be debated, but the sequence is sure to follow. I believe that the recognition of birth control must be a corollary of an intelligent public health policy and practice in any country. It is the individual's right to regulate the size of family, and the nation's responsibility to influence the size and character of its population in accord with national welfare, by such measures as health and medical protection, immigration control and the furtherance of eugenics. So much for an attempt at a public health philosophy as applied to India. I believe that responsibility for the preservation of life and promotion of health in this country may be accepted as being in accord with reason and logic, as well as with humane sentiments.

The question of the proper relationship of the health and medical organizations to each other arises in most countries, as it does in India. Whether they should be united or separate is often a subject of discussion and debate. There are advocates for each policy; some argue that preventive medicine should be completely divorced from curative medicine, and others maintain that they overlap to such an extent that they are inseparable. Some administrators would place their health programmes under the general medical administration. There are instances where a national health administration or Ministry of Health is the parent organization, within which hospitals, dispensaries and medical practice are administered or controlled. In the history of medical care in India, it is obvious that treatment of the sick was the first development and medical relief and disease control have been the primary consideration. The office of a Sanitary or Public Health Commissioner and his activities in the field of public health or preventive medicine were more recently established. In the Provinces and States, there is, I understand, in most cases a definite demarcation between the services. The Central as well as the Provincial governments are beginning to question whether these services should be distinct and separate, or parallel and co-ordinated, or even whether there should not be a true amalgamation in both supervision and field application.

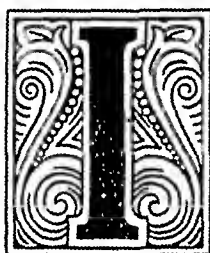
Those who favour a distinct separation present the argument that by limiting one organization to preventive work, there is less chance of losing sight of the primary objective which is to prevent rather than to cure or palliate disease. In favour of combined services, the arguments are that such a service is more economical, prevents duplication and overlapping, and facilitates co-ordination. The choice or decision in this question is usually determined in practice by certain conditions, namely, the number and distribution of available medical and auxiliary personnel, the economic capacity of the people to support one or two branches, and the spirit and temper of the people; that is, whether they are individualistic or community-minded in this respect. In the United States, before the war,

there was approximately one doctor per 800 inhabitants. The standard of living is relatively high, and the spirit of individual choice is strong among doctors and the public. Under these conditions there is usually a distinct separation between health and medical services. It is still the policy of the organized medical profession to preserve the right to private practice, and of the individual to choose his physician and medical service. The application of public health is a government responsibility which conflicts only occasionally with the medical services, which are largely private. However, we, in the United States, are evolving slowly towards a larger degree of combined services and community efforts to meet medical needs. I believe England follows also a middle-of-the-road course. Measures of social insurance and social security are growing in most countries with favourable economic standards, and are becoming available to a larger proportion of the population.

In China the question has been settled. State medicine or the union of preventive and curative measures under public auspices is the accepted national policy. That there are only 5,000 to 6,000 qualified doctors in China to serve the many millions is undoubtedly a factor in the decision; also the authorities are convinced that public health and medical services can be most efficiently rendered as a combined service. In the cities of China there is still a considerable number of private practitioners, but at least 70 to 80 per cent of the graduates of the better medical colleges are in State service. An interesting and important thing about the situation in China is that medical assistance, given through the health organizations, has not detracted from the major interest and goal of prevention. This attitude may be attributed to the leaders who maintain the concept that public health in its larger sense is the dominating consideration. A proper balance is also maintained between prevention and medical care. Medical undergraduates are taught hygiene and preventive medicine as an integral part of their medical education, and not merely as an isolated and supplementary course. The graduate is thus less apt to be submerged by the interests and needs of curative work.

It is my tentative view that a policy of united and correlated health and medical services of India, at least in rural areas, is logical and desirable. Perhaps I should interpolate some remarks on the health units, which our organization has been instrumental in assisting in several States and Provinces of this country, as well as in Ceylon. These health units in India have been on a standard form serving approximately 40,000 people, and their activities have been limited to preventive or public health service. I have had occasion to appraise their results recently. On the credit side these units have been useful experiments and demonstrations in rural hygiene. They have been utilized as necessary and desirable practice fields for the

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training of health personnel. On the critical side, the staffs have not appeared to be sufficiently qualified for such demonstrations, and health visitors are, unfortunately, not public health nurses; supervision has been limited; the annual *per capita* cost of 12 annas seems to have proved more expensive than the local authorities could or would support when outside aid was withdrawn. Judgment may also be assessed on the fact that little if any extension of health unit programmes beyond the original demonstrations has been observed. Perhaps an explanatory factor is that, as purely preventive units, they have been found expensive when in the same area medical and other social services were non-existent and elementary education was woefully inadequate. After this useful experience, it seems desirable that the matter of local health services should be carefully re-studied. A careful experiment made in accord with the suggested policy of uniting and correlating the health and medical services would be useful. Some steps in this direction are being taken.

In this country, there are reported to be about 42,000 doctors. Although this number is many more than in China, the average is still not much greater than one per 10,000 inhabitants. Since there are even fewer doctors in the rural regions, it is questionable if a dual service can be expected or supported. The risk in combining the medical and health services is that they may become 95 per cent curative organizations. If such a union is to succeed and maintain a proper balance of activities, leadership in administration both in the central and the local directions must be a determining factor. It is essential that the responsible officers should have a solid foundation in the concepts of public health and preventive practice. I am not sure that the medical colleges in India have reached a stage in which public health education, either as graduate or under-graduate study, has given the average graduate the proper perspective toward prevention and cure. There is need for further study and experimentation with this problem.

Another impression which comes from contact with the official administrations in India may be touched upon briefly. The relative degree of centralization or decentralization of authority in public health and medical administration is an influence in determining the efficiency and rapidity of the public health movement. That India is markedly decentralized in this branch of government is apparent, although the Central Government has authority in federal public health questions and considerable influence in medical education and medical administration of the Provinces and States. By the Acts of 1919 and 1935, a large measure of responsibility was transferred to local administrations. In view of the geographical extent and political complexities of the country, such decentralization is presumably inevitable and reasonable. On the other hand, I understand that many Provinces and States have in turn passed on their health and

medical responsibilities to the smaller local bodies. To transfer such responsibility and initiative to the smaller units was, of course, the easiest procedure, but not necessarily the most effective. Until the educational level of the people and the spirit and understanding of their leaders are sufficient to cope with these problems, such peripheral decentralization is apt to be a non-progressive measure. The maintenance of control of the major health and social services in the hand of the larger units of the Provinces and States or their principal subdivisions will probably be a safer and more effective policy for some time.

The effectiveness of public health and medical services in any country depends basically on the quantity and quality of its personnel. This leads to a consideration of the different categories of technical personnel and their education. It refers to medical men, sanitary engineers and inspectors, nurses and midwives. My knowledge of details of their training and practice is still so limited that I am not competent to appraise the situation fully. However, I am bold enough to remark on a few major impressions as a newcomer. Since there are upwards of 40,000 doctors including licentiates, and an annual production of 700 graduates and 1,000 licentiates, it suggests that the quantitative needs of India are met in a greater measure than in some other Far Eastern countries, though the supply is still inadequate for the total population. The quality of medical education is another matter. I hesitate to say more than register a preliminary impression of its mediocrity. Post-graduate medical education, academic research and public health teaching to under-graduates appear to be limited in scope and accomplishment. There has been perhaps too much encouragement for study abroad as the only route to advancement and progress, and too little encouragement for the development of one or two outstanding institutions of medical teaching in the country itself.

Important associates of the doctor, in the field of sanitation, are the sanitary engineer and the sanitary inspector. India depends apparently on her civil engineers and foreign-trained engineers in this field. In general, I judge that the level of training and competence of sanitary inspectors leaves much to be desired, and they are not up to the standard of other areas of British administration.

To express a personal view, nurses are the backbone of effective medical service and public health practice. Although there are numerous schools of nursing and about 7,000 nurses in India, this profession is in a more backward stage than the other medical classes. The explanation lies, of course, in the obstacles of language, custom and social circumstances which have restrained women of desirable classes from participating more fully in this important work. It is believed that India is ready to advance in this essential part of public health, and the need is urgent. The nursing profession must call on

the better classes of Indian womanhood, and should attempt to draw into nursing some of the women who undertake medical study. India needs leadership among Indian as well as European women. I wonder if an adequate effort has been made to stimulate and find such leadership.

According to my information, there are about 500 health visitors in this large country. Although this class of health worker is a step in the right direction of prevention, their number is woefully small and most of their activity is limited to maternity and child welfare. The emphasis on midwifery as a pre-requisite for the health visitors may have a reasonable foundation, but it restricts also the class of women who are enlisted. A strange finding for a new-comer, experienced in public health organization in other countries, is the discovery of the non-existence of public health nursing.

Lastly, I may offer some comment on the relation of public and private agencies in the field of public health. It is frequently a question as to what are the proper spheres of private endeavour and what should be the responsibility of the public administrations. We are perhaps wise if we start with the accepted principle that public health is a fundamental function and responsibility of government. Government, either Central or local, may at times choose to delegate its responsibility in a given field by agreement or tacit understanding to a private or semi-official agency. Private organizations and societies are accustomed and fitted to initiate and demonstrate, to lead the way in new undertakings of health and medical services. Many pioneering accomplishments have been achieved through such unofficial efforts, but ultimately the responsibility should be brought to government. To take advantage of voluntary services, to raise funds, and to administer without bureaucracy, are characteristics which have enabled private societies to contribute and set examples for the public health movement in many countries. On the other hand, there is a danger that once a private organization has undertaken a particular health programme, this activity may become a vested right, and directors and staff hesitate to transfer their responsibility to constituted authority.

Again as a new-comer, I am impressed by the multiplicity of associations, societies and funds which one meets in India. Such organizations which engage in public health activities, health teaching, and medical assistance are usually a stage in the development of public consciousness and should lead ultimately in most cases to government administration of those activities. They serve the useful purpose of stimulation and demonstration. Their pioneering spirit may set the example until public agencies can be persuaded to undertake the full responsibility. If private organizations continue to guard indefinitely such activities from government, there may

be the plausible charge of paternalism in health and medical administration.

It is a departure from the practice of most countries that the Indian Red Cross has assumed or been assigned most of the maternity and child welfare work in this country. The bureau service in reality is a form of government organization. This arrangement has presumably resulted in competent administration and greater progress in this important field of public health. After a certain stage, the question arises as to when government agencies, central or local, will take over their responsibility? I noted with interest a recent article by the Director of the Bureau upon the functioning of a central maternity and child welfare department and urging the desirability that both Central and Provincial governments have their own departments of maternity and child welfare. Such a proposal appears logical and may be anticipated as a normal outcome in the evolution of public health administration.

Most of the world is now engaged in war. Many departments of the medical and health services of this country are devoting themselves to aiding that effort in every possible way. Public health and physical fitness are increasingly important in wartime; fortunately the budgets of medical and health services are less apt to be sacrificed than some others. New developments which require additional personnel or expenditures may have to be deferred. There is already considerable discussion and some planning for peace and post-war reconstruction. It is not too early for planning the future of public health and medical services in India. I have been impressed by the activities of the Central Advisory Board of Health which began so auspiciously a few years ago. The planning and advisory function of this board has already justified itself and should play an increasingly important rôle in the future. Planning by individuals, groups, and government is seriously needed in the field of public health and particularly in co-ordination with the other social services.

Current Topics

Treatment of Shock by Direct Action on the Vegetative Nervous Centres

By LENA C. STERN, M.D.

(From the *British Medical Journal*, 7th November, 1942, p. 538)

THE MECHANISM OF TRAUMATIC SHOCK

Efforts to produce shock experimentally play an important part in the elucidation of the mechanism of traumatic shock. The criteria of shock conditions in all these experiments were: (1) sudden and persistent fall in blood pressure, with a rapid and feeble pulse, (2) shallow breathing, (3) the absence of reaction on irritation, (4) lowering of the temperature. All this points to a disturbance of the vegetative nervous system, particularly the sympathetic, which in itself leads

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to a diminution of volume of the circulating blood, due to the accumulation of blood in the blood depots and diminution in the liquid part of the blood from plasmorrhœa. This disturbance of the vegetative nervous system is also a cause of chemical changes which characterize the course of shock (appearance of acidosis, diminution of glucose, etc.). This work also showed that with the weakening of the sympathetic nervous system there is a stimulation of the parasympathetic system which shows itself by a number of inhibitive effects.

Experiments made by us and our colleagues (Rosin, Chvoles) have proved that sensitivity, especially to pain, plays an important part in the development of shock. They showed that irritation of the skin by an induction current for 2 to 6 hours causes shock, whereas with preliminary anesthetizing of the skin with novocain much longer electrical stimulation is without effect. Given the same conditions, shock is most easily produced by irritation of the skin on the inner surface of the thigh, the peritoneum, and the periosteum, whereas irritation of the dura even for as long as 8 to 12 hours does not cause shock. The rhythm of irritation is important, shock usually appearing much more quickly when the rhythm is quicker.

The significance of the preceding conditions for the development of shock in man has been proved by clinical observations. Excessive tiredness, prolonged insomnia, insufficient nourishment, fear, exposure, loss of blood, and, not least, painful irritations, lead, after transient overstimulation of the sympathetic nervous system, to its exhaustion and thus facilitate shock. The results of these experiments show that shock is caused, apart from loss of blood, by a whole complex of circumstances connected with a definite condition of the nervous centres. Only when all these conditions are present does shock develop. In clinical studies of shock, attention has been mainly directed to the functional state of the peripheral organs, such as the cardiovascular and respiratory organs. A more detailed analysis, however, has shown that all these cardinal changes, including the changes in metabolism and in the physical and chemical state of the blood and the tissues, are not actually specific to shock. In fact, similar changes, such as a fall in blood pressure, diminished nervous reactions, etc., can be caused by a depression of the sympathetic nervous system such as occurs also in other pathological states. All these changes form a syndrome which characterizes shock and shock-like conditions and can be caused by action on the vegetative centres; this points to the important part played by the central nervous system in the production of shock. It therefore follows that in order to be able to understand the mechanism of shock and to apply useful therapy and prophylaxis one must concentrate on the functional conditions of the nervous centres, on their metabolism, and, in conjunction with this, on the character of the cerebrospinal fluid, i.e., their immediate nourishing medium.

FUNCTION OF CEREBROSPINAL FLUID

The importance of the cerebrospinal fluid to the functioning of the nervous centres has been shown by observations in laboratories and clinics for many years. These observations have proved that the cerebrospinal fluid (taken in its broad sense as the fluid which fills not only the ventricles of the brain and the sub-arachnoid space, but the whole of the perivascular and pericellular spaces of the brain tissue) is the immediate nourishing medium of the central nervous system. The chemical composition, as well as the physical, chemical, and biological character, of the cerebrospinal fluid mainly depends on, and is determined by, a special mechanism—the so-called hæmato-encephalic barrier. The anatomical substratum of this barrier is, apart from the vascular plexus, the capillaries and pre-capillaries of the brain, in the first place their endothelium. The hæmato-encephalic barrier has a great selective capacity, on account of which not all substances which normally circulate in the blood, or get there accidentally, pass from the blood stream into the c.s.f. There takes place 'a certain choice' as the result

of which a relative constancy of the composition of the c.s.f. is maintained, and there is a certain independence of possible changes in the consistency and quality of the blood.

It has been shown that not only the introduction of abnormal substances from the blood into the c.s.f., but even a simple disturbance of interrelations between the normally existing substances in the c.s.f., such as between certain electrolytes, causes a more or less severe reaction in the nervous centres which sometimes leads to the death of the animal. In certain cases we were able to notice that definite changes in the c.s.f. are accompanied by some features which resemble the complex of symptoms characteristic of shock and similar states. This particularly applies to the ions of Ca and K. It was shown that change in the concentration of these ions in the c.s.f., leading to a change in the coefficient K/Ca , has a very strong influence on the condition of the central nervous system, particularly on the vegetative centres. For example, the introduction of minimum doses of Ca salts directly into the c.s.f., especially into the ventricles, brings about in the animal a condition of severe depression, whereas the introduction of minimum doses of K salts produces pronounced excitement. This suggests that the direct cause of the change in the functional condition of the cerebrospinal system may be a corresponding change in the composition of the c.s.f. Comparing the occurrence in shock of changes in the different physiological systems, particularly in the cardiovascular and respiratory systems, with the action which causes a stimulation of the vegetative nervous system, we conclude that the sympathetic and parasympathetic nervous centres play the most important part in the production of shock. The cause of changes in the vegetative nervous centres may be strong irritation coming from the periphery. The intensity of effect brought about by such irritations depends on the preceding condition of the vegetative centres (their greater or lesser excitability and reactivity), which in itself is closely connected with the chemical composition of the c.s.f.

The possibility of varying the reaction of the sympathetic and parasympathetic centres by introducing into the cerebrospinal canal certain substances such as K salts and Ca salts points to the influence of the electrolytic composition of the c.s.f. on the condition and activity of the vegetative nervous system. Diminished tone of the sympathetic centres causes those disturbances of function characteristic of shock, and especially of the hæmodynamics, the disturbance of which is quite sufficient to bring about in different physiological systems those changes which characterize shock. It is therefore understandable that all efforts to combat the signs of shock are mostly directed to the re-establishment of circulation and the normal action of the cardiovascular system.

FAILURE OF SHOCK THERAPY

However, the ordinary methods of fighting shock generally do not give positive results, because they do not influence the condition of the central nervous system. These negative results are explained to a great extent by the presence of the hæmato-encephalic barrier.

As regards certain medicinal substances, it has been noted that, introduced into the circulation, they have no effect on the central nervous system, whereas the introduction of minimal quantities of the same substances directly into the cerebrospinal canal, particularly into the ventricles, often has a marked effect. The conclusion, therefore, is that in order to obtain a positive effect one should introduce the substance intrathecally. The action of a substance admitted into the general circulation differs from the action of the same substance introduced straight into the c.s.f. This applies particularly to those substances which are normally present in the c.s.f. and the blood, such as K and Ca salts and some hormones. Many experiments have proved that there is an antagonism between the central and peripheral parts of the vegetative nervous system as regards their reaction to the same substance. This antagonism more or less explains the

absence of a positive anti-shock action of the medicinal substance when introduced straight into the circulation. Actually, if these substances do penetrate into the central nervous system, particularly the vegetative centres, they may produce an opposite effect and thereby neutralize the immediate action which they have produced on the peripheral vegetative organs. It follows, therefore, that in order to understand the action of a given substance one must take into consideration not only the permeability of the hæmato-encephalic barrier for this particular substance, but also the fact that the substance which easily passes through the hæmato-encephalic barrier into the c.s.f. may, on contact with the vegetative centres, cause an action which is opposite to the one on the peripheral organs. There is, therefore, an interference, and the final effect may be negligible or even opposite to the one expected. To produce a direct action on the vegetative nervous centres one must administer the substance directly into the c.s.f.

One must add that a positive effect can be obtained only in cases in which the given substance is introduced into the ventricles of the brain, whereas the introduction of the substance into the subdural or subarachnoid spaces is usually without effect because it passes rapidly from the c.s.f. into the blood stream and does not come into contact with the nervous centres.

INTRAVENTRICULAR INJECTION OF K SALTS

Laboratory experiments (Chvoles) have shown that in many cases of experimental traumatic shock the direct injection into the c.s.f. of a solution of K salts gave a positive result. In most of the experiments the signs of shock disappeared very quickly, the blood pressure rose rapidly to normal, the rhythm of respiration became normal, as also the reactivity and excitability of the animal.

It is interesting to note that in those cases in which trauma was accompanied by a severe loss of blood (up to 50 per cent) the introduction of potassium phosphate into the c.s.f. without a preliminary blood transfusion brought the animal out of shock, whereas in control experiments the introduction of a physiological solution as well as a transfusion of blood had no effect. It appears, therefore, that under the influence of increased excitability of the sympathetic centres there is a mobilization of the blood from the depots and simultaneously a transference of fluid from the tissues into the blood, as a result of which the volume of the circulating blood is increased.

The best results have been obtained by injecting potassium phosphate directly into the lateral ventricles or into the cisterna magna, provided that definite rules are followed. If these rules are not observed, the injected fluid often does not reach the cerebral ventricles, but, following the normal flow of the c.s.f., passes into the subarachnoid space without reaching the vegetative centres. The introduction of the fluid into the subarachnoid space does not produce the necessary effect, because it passes into the blood stream very quickly without coming into contact with the nervous centres. It can now be positively stated that by fulfilling the necessary conditions as regards concentration, temperature, and reaction of the solution of potassium phosphate, as well as the rules of technique of its introduction into the cerebrospinal canal (i.e., the ventricles), a definite effect can as a rule be obtained. It is obvious that a positive action of potassium phosphate on the vegetative nervous centres is possible only if the centres have still retained the ability to react. Completely exhausted vegetative centres which have lost their reactivity cannot be re-established by this method.

Taking into consideration the fact that the introduction of potassium phosphate into the cerebrospinal fluid increases the tone of the sympathetic centres, its use is indicated in those cases in which symptoms of weakened tone are present. Irrespective of whether we deal with shock or a shock-like condition, we cannot possibly expect any useful effect in cases in which there is an anatomical injury to the vegetative centres. An

effect can be expected only in a purely functional disturbance of the vegetative nervous system.

The time factor is of great importance. One obtains the best results in cases when the potassium phosphate is introduced into the ventricles of the brain within a short time after the appearance of shock. This applies not only to traumatic shock but also to anaphylactic, peptone, and histamine shocks. This can be explained by the fact that the exhaustion of the vegetative centres gradually increases, and when it reaches a certain stage the possibility of stimulating them by any method disappears.

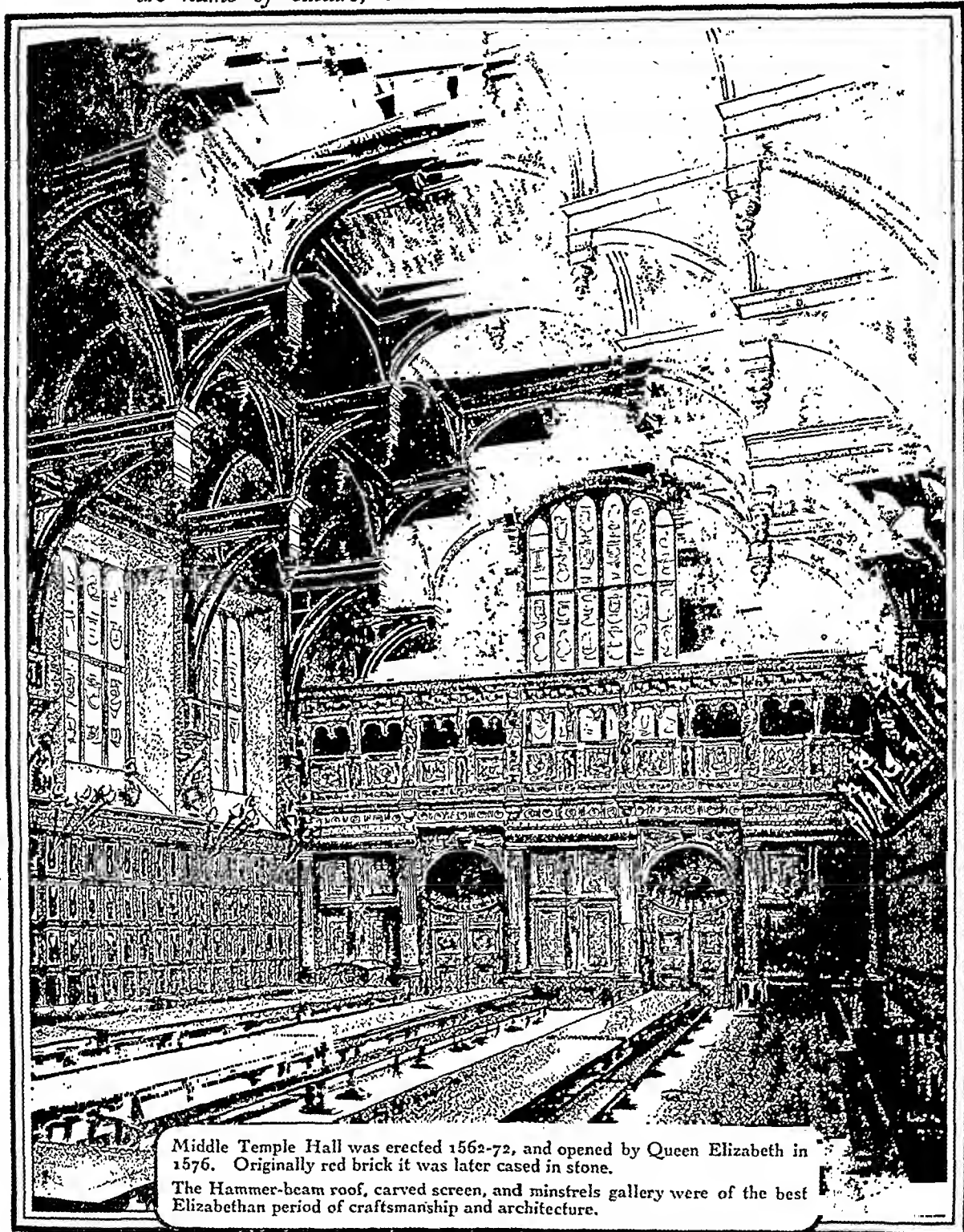
The results obtained by laboratory methods have been fully corroborated by clinical experience and at the front. To obtain a positive effect 1 c.cm. of a solution of potassium phosphate in a concentration of 1/6 gramme-molecule, with pH of 7.6, was found best. Introduction of potassium phosphate into the lateral ventricles not only increases the concentration of potassium but also diminishes the concentration of the Ca ions, which leads to a considerable increase in the co-efficient of the K/Ca ions. When the potassium phosphate is injected, one must remember the necessity for rapid penetration into the ventricles so that direct contact may be obtained with the vegetative nervous centres. Laboratory experiments, as well as clinical observations, have shown the importance of the preceding condition of the sick or wounded, particularly the increased excitability of the nervous system in the development of shock. In prophylaxis it is rational to counteract the increased excitability so as to prevent exhaustion, which causes shock; by giving sedatives, and blood transfusion when there is loss of blood. To prevent a possible relapse this prophylaxis can be successfully applied also in the initial stages of shock, as well as after the shock has disappeared. The first condition for preventing a repetition of shock syndrome in traumatic shock is the removal of the direct cause of shock, particularly the source of painful sensations, as, for example, by local anaesthesia. Fluid can be introduced into the ventricles of the brain by way of cisternal puncture. The following rules must be observed.

TECHNIQUE OF CISTERNAL INJECTION

The patient must be in a horizontal position (preferably on his left side); the head must be lower than the body and bent on to the chest; the lower limbs must be flexed (a position similar to Trendelenburg's). The landmarks are the external occipital protuberance and the first cervical spinous process. These landmarks are felt on the back of the head, which has been shaved and thoroughly disinfected. One fixes with a finger the skin between these two points and inserts the needle exactly in the midline at the level of the external auditory meatus. Sliding along the occipital bone one reaches the atlantoid membrane. The moment this membrane is perforated one hears a crackling sound. For this puncture one may use a graduated cisternal needle or an ordinary lumbar puncture needle. As a preliminary measure one estimates the length which corresponds with the depth of the puncture (from 4 to 5 cm.). The criterion that the needle has penetrated into the cisterna magna is the appearance of translucent c.s.f., which escapes from the needle after removal of the stylet. On account of weak pressure in shock conditions the c.s.f. very often does not appear spontaneously and has to be drawn out by a syringe. After 1 to 2 c.cm. of the c.s.f. have been withdrawn with a syringe, 1 c.cm. of the solution of potassium phosphate, which has been warmed to body temperature, is injected with a syringe under a definite pressure, so that it penetrates into the ventricles. This method of treatment is very easy and can be applied at the front. The preparation of the potassium phosphate solution is not complicated, but must be done very carefully. The glass of the ampoules must be neutral. The solution is a mixture of the monometallic and bimetallic potassium phosphate (concentration 1/6 gramme-molecule), and can be prepared either from these salts (K_2HPO_4 and

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KH_2PO_4) or by adding the orthophosphoric acid to a solution of corrosive potassium up to pH 7.6.

As a rule the effect of this injection takes place in 1 to 2 minutes or even sooner (i.e., in the first place the blood pressure rises and the respiration becomes deeper). The absence of effect within a few minutes is generally due to the fact that the fluid has not reached the ventricles, as a result of the incorrect direction of the needle or of insufficient pressure. In these cases one must repeat the operation. When toxæmia is threatening—i.e., when toxic substances which form in the injured tissues enter the blood—the further formation of these substances must be stopped by excising the injured parts where possible; positive results, which are obtained by the direct action of potassium phosphate on sympathetic nervous centres, do not exclude the possibility of the appearance of toxæmic shock later on.

CONCLUSIONS

1. In the last phase of traumatic shock there is first of all a considerable fall in the tone of the sympathetic nervous system and a partial rise in the tone of the parasympathetic nervous system.

2. The most effective way of combating traumatic shock in its later phase is to raise the tone of the sympathetic centres by direct action on the vegetative centres; potassium phosphate simultaneously raises the tone of the sympathetic centres and lowers the tone of the parasympathetic.

3. By direct action on the nervous centres the ionic potassium causes an excitability of the sympathetic nervous centres, whereas the ionic phosphates, by concentrating the ionized Ca, cause a diminution of the tone of the parasympathetic nervous centres.

4. A direct introduction of potassium phosphate into the cerebrospinal canal contributes to a quicker action of this substance on the nervous centres and at the same time obviates the possibility of its opposite effect on the peripheral part of the vegetative nervous system.

5. The use of potassium phosphate as an anti-shock remedy is indicated in all those cases in which there is a diminution of the tone of the sympathetic nervous centres, such as a fall of the blood pressure, a lowering of cardiac activity and respiration, diminution of excitability, reactivity, etc.

6. Potassium phosphate must never be used in cases in which there is increased excitability of the sympathetic nervous centres, such as sometimes occurs in the first stage of shock.

7. If hæmorrhage is present it must be arrested by all available means, because the considerable rise of the blood pressure through the introduction of potassium phosphate will definitely increase hæmorrhage.

8. To avoid a repetition of shock it is necessary after the introduction of potassium phosphate to remove the actual cause of shock, in particular painful stimuli.

9. To ensure the direct action on the vegetative nervous centres, which are situated in the ventricles of the brain, potassium phosphate must be introduced directly into the ventricles. This is done by means of cisternal puncture. The fluid must be introduced with a definite pressure and the direction of the needle must be correct. The position of the patient must be horizontal, preferably on the left side, and the head must be lower than the body.

10. One must act quickly, without loss of time, so as to avoid a complete exhaustion of the vegetative centres.

11. The introduction of potassium phosphate does not exclude all the other measures against shock, especially blood or plasma transfusion.

12. Blood transfusion must be done in all cases where there is marked loss of blood. In other cases a blood transfusion is not absolutely necessary.

Reviews

SURGERY OF MODERN WARFARE.—Edited by Hamilton Bailey, F.R.C.S. Compiled by 72 contributors. Volume I. Second Edition. 1942. (Complete in Two Volumes.) E. and S. Livingstone, Edinburgh. Pp. xvi plus 480, with 375 illustrations. Many in colour. Price, 40s. Postage, 9d.

THE new edition of *Surgery of Modern Warfare* is very welcome at this juncture in the war. The new techniques and new procedures are beginning to take more definite shape. In the first edition there was considerable evidence of immaturity which has now disappeared. It is perhaps rather patronizing to say this of many of the well-known writers, but nobody should be ashamed of learning, and obviously many of the writers have learnt a considerable amount since the first edition was published. It now appears in two volumes of which we have as yet only received the first; presumably the second one will be on its way. The quality of the production seems not to have suffered at all on account of paper shortage or other difficulties.

THE PRINCIPLES OF NEUROLOGICAL SURGERY.—By Loyal Davis, M.S., M.D., Ph.D., D.Sc. (Hon.). Second Edition. 1942. Henry Kimpton, London. Pp. 503 with 154 engravings, containing 298 illustrations and 5 coloured plates. Price, 35s.

IN the comparatively short space of 500 pages, the author of this excellent book takes from the vast field of neurology those sections which touch upon the realm of the surgeon, and in masterly style builds them up from their foundations of anatomy, embryology, physiology and pathology until the whole vista of surgical possibilities stands out with a clarity not easily attained in this wide and complicated subject. The object of this work is not to provide a textbook of neurological surgery, but to provide a guide for the judgment of practitioners and others who are not specialized in these particular fields.

Apart from surgery, the volume provides an excellent dissertation upon the anatomy, physiology and pathology of many parts of the central nervous system and its peripheral extensions, and in no part is this more exemplified than in the chapter on cerebral tumour. Statistically, this section is based upon the author's personal experience of nearly 650 cases, and these are classified, their genesis discussed, and their clinical manifestations described in masterly style.

The opening chapter is concerned with the eliciting and interpretation of many of the clinical signs, and this is followed by a useful chapter on cranio-cerebral injuries; here the physiology of the fluid circulations within the skull is set forth, and the reader is led to correlate the complex problem of contusion, concussion and irritation, and to use this as a basis for the consideration of every problem upon its individual merits.

The section dealing with cerebral abscess is somewhat brief, and the conflicting procedures discussed for treatment of this condition, indicate the imperfection of our knowledge.

A considerable part of the work deals with injuries and other lesions of the spinal cord, and this is followed by a most valuable chapter on the injuries of peripheral nerves, their repair and prognosis. There are many other chapters dealing with such matters as visceral pain, the rôle of surgery in lesions associated with the autonomic nervous system, and in the various developmental anomalies of the cerebral nervous system itself.

The final section, dealing with the rôle of surgery in the treatment of essential hypertension, appears somewhat redundant to the purpose of the book, and certainly its length appears excessive, though its discussion is an able one backed by much personal experience.

The work is well illustrated with photo-micrographs, clinical photographs and with good x-ray reproductions; the style and composition are beyond reproach, and

the whole can be strongly recommended to both physician and surgeon.

C. M. S.

MIDWIFERY.—By Ten Teachers. Edited by Sir Comyns Berkeley, Clifford White, and William Gillatt. Seventh Edition. 1942. Edward Arnold and Company, London. Pp. viii plus 562. Illustrated. Price, 18s.

THE seventh edition of this valuable work has made its appearance, and is in keeping with the excellence of the former impressions.

Some new matter, notably on the most recent treatment of ante-partum hæmorrhage, the latest classification of abnormal pelvis, and the use of the sulphonamide group of drugs, has been added. Some redundant matter has been removed and the chapters have been re-arranged, with the result that the number of the chapters has been reduced by two, and the pages by one hundred and ten.

The original wish of the Ten Teachers that their book in subsequent editions may continue to be of service, is amply fulfilled.

H. E. M.

DISEASES OF WOMEN.—By Ten Teachers—under the direction of Clifford White, M.D., B.S. (Lond.), F.R.C.P. (Lond.), F.R.C.S. (Eng.), F.R.C.O.G. Edited by Sir Comyns Berkeley, Clifford White, and Frank Cook. Seventh Edition. 1942. Edward Arnold and Company, London. Pp. viii plus 435. Illustrated. Price, 18s.

THIS well-known textbook, of which the 7th edition has now been published, presents the essentials of the subject in a clear and concise manner. The joint editorship by ten outstanding teachers has eliminated the personal factor, and has resulted in the production of a particularly well-balanced survey of the field. Its reputation is established as a good students' handbook.

In this edition the chapters on inflammatory conditions have been revised in the light of recent advances in sulphonamide therapy, but one finds no reference to the treatment of chronic pelvic inflammation by the non-specific protein therapy so much used in this country.

The book contains a good chapter on 'neurasthenia' and 'neurosis in relation to pelvic disorders', which contains much wise advice for the practitioner. This is an aspect of the subject too often neglected in the student's education, and the inclusion of such a chapter in a student's textbook is a welcome sign.

In addition to descriptions of the major procedures of gynaecology, this book contains many useful minor hints, and can be thoroughly recommended as a very sound smaller textbook of its kind.

M. N.

ADVICE TO THE EXPECTANT MOTHER ON THE CARE OF HER HEALTH AND THAT OF HER CHILD.—By F. J. Browne, M.D., D.Sc., F.R.C.S.E., F.R.C.O.G. Sixth Edition. 1942. E. and S. Livingstone, Edinburgh. Pp. 51. Price, 6d. Postage, 2½d.

THIS might well be called the Expectant Mother's Guide, for in it is set down, in less than fifty pages of print, in language readable and unambiguous, all that the expectant mother needs to know in order to be able to look forward to the birth of the child with informed confidence.

In the chapter 'Benefits of Antenatal Care' are explained simply the chief dangers which must be anticipated during pregnancy and labour in a small percentage of cases, and the extent to which sound prenatal care started early in pregnancy will protect mother and infant. In this chapter, as throughout the booklet, advice regarding care is naturally based on the facilities and staff now available for the welfare of pregnant women and infants in Britain under the terms of recent legislation. This limits the applicability to Indian conditions, and further emphasizes the need for a similar type of publication produced in this country.

The hygiene of pregnancy is equally well presented, and there is an excellent chapter on 'Common Disorders of Pregnancy and Their Treatment'. Chapter VII, devoted to the feeding and care of the baby, contains much useful information for the young mother. A sound book also for the medical student, the health visitor, and the midwife.

L. G.

DISORDERS OF THE BLOOD: DIAGNOSIS, PATHOLOGY, TREATMENT AND TECHNIQUE.—By Lionel E. H. Whitby, C.V.O., M.C., M.A., M.D. (Cantab.), F.R.C.P. (Lond.), D.P.H., and C. J. C. Britton, M.D. (New Zealand), D.P.H. Fourth Edition. 1942. J. and A. Churchill, Limited, London. Pp. xii plus 595, with 12 plates (8 coloured) and 59 text-figures. Price, 28s.

THIS book has gone through four editions in seven years. We are not at all surprised at this as it has been accepted as the standard book on hæmatology for British readers. The present edition is brought up to date, or shall we say, as up to date as it is possible in these difficult times. As the writer points out, there are considerable difficulties in writing a book in war time; not the least of these are the facts that all foreign literature is very irregular in its arrival and that, from the countries with which we are at war, of course it does not arrive at all.

The only traces of the war and the paper restrictions that we can see in the book are that the plates have had to be printed back to back in some instances, so that they are not always in their appropriate places, and that perhaps the paper is not quite of the same quality as in earlier editions.

HEART FAILURE.—By A. M. Fishberg, M.D. Second Edition. 1940. Henry Kimpton, London. Pp. 829. Illustrated with 25 engravings. Price, 40s.

IN this edition Dr. Fishberg has incorporated the results of latest clinical and experimental investigations on circulatory failure. This has necessitated some changes in the text and size of the book. In the opening chapters, recent work on circulatory variables, such as cardiac output, velocity of blood flow, venous pressure and the circulatory blood volume is reviewed, and the author clearly explains how observations on these factors have contributed to the elucidation of the manifestations of heart failure. The clinical picture of the signs and symptoms of this condition with their pathogenesis are then described in a clear manner, each of them being taken and discussed separately. The various forms of heart failure are considered in detail and there is a chapter on peripheral circulatory failure and shock which though more often encountered as a result of trauma and other conditions, also occurs in some forms of heart disease. About 140 pages are devoted to therapeutics which has been discussed in a systematic manner, including the general management of heart failure, the use of digitalis, diuretics, oxygen, etc., and the treatment of individual diseases with heart failure. These pages provide a basis for the rational and critical judgment of modern therapeutic agents and measures.

The book is essentially clinical in its outlook and is one of the best works on circulatory diseases. Although a long book, it is warmly recommended to all practising physicians.

R. N. C.

A TEXTBOOK OF BIOCHEMISTRY FOR STUDENTS OF MEDICINE AND SCIENCE.—By A. T. Cameron, M.A., D.Sc. (Edin.), F.I.C., F.R.S.C. Sixth Edition. 1942. J. and A. Churchill, Limited, London. Pp. viii plus 376, with 3 plates and 25 text-figures. Price, 18s.

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Dr. Cameron's book needs no introduction, not only because it has gone through five previous editions but also because it has been a standard textbook for students.

The present edition serves to show that the author has had to work hard to bring the rapidly changing subject as up to date as possible. This has necessitated a thorough revision of almost all the chapters of the book. The sections dealing with the vitamins, diet and intracellular respiration have, in particular, been thoroughly revised and largely rewritten. The important recent work on the chemical nature of many crystalline viruses has been discussed, and further evidence favouring the view that many viruses are single chemical compounds has been quoted.

The book is a mine of information and gives much valuable and up-to-date knowledge. It is a valuable contribution to biochemistry and we have no hesitation in recommending it as such.

J. P. B.

THE DIABETIC A.B.C. WAR-TIME SUPPLEMENT.—

By R. D. Lawrence, M.A., M.D., F.R.C.P. (Lond.). Second Edition. 1942. H. K. Lewis and Company, Limited, London. Pp. 15. Price, 9d.

THE war supplement to Dr. Lawrence's Diabetic A.B.C. is no doubt a great boon to the numerous diabetic patients particularly in countries where air raids are frequent and involve increased danger to diabetics. This book, in giving simple and practical instruction, warns them against such dangers, particularly the danger of severe cases missing even a single dose of insulin.

The problem of diabetic diet arising from the compulsory rationing, as also the modification of the dosages of insulin necessitated thereby, has been fully discussed in a very helpful manner.

J. P. B.

A SYNOPSIS OF HYGIENE (JAMESON AND PARKINSON).—By G. S. Parkinson, D.S.O., M.R.C.S., L.R.C.P., D.P.H., Lieut.-Col., R.A.M.C. (Ret.). With a section on personal hygiene. By G. P. Crowden, D.Sc., M.R.C.S., M.R.C.P. Seventh Edition. 1942. J. and A. Churchill, Limited, London. Pp. viii plus 712, with 16 illustrations. Price, 25s.

A Synopsis of Hygiene is a very well-known book which is now accepted as the standard book in Great Britain; it has been brought up to date by the junior author. Sir Wilson Jameson is obviously too busy with his work at the Ministry of Health to allow time for this sort of thing, but the revision has been carried out very efficiently by Col. Parkinson with the help of Dr. Crowden of the London School of Hygiene and Tropical Medicine.

It is too early yet to see the effect of the war on the public health in Great Britain in proper perspective, but it is obvious that very considerable changes in the whole picture will result. Considerable immediate effects have been felt during the worst air raid years and have entailed new health measures. This aspect has been dealt with shortly, as it can only be at present, but readers will find this short section very helpful.

THE SANITARY INSPECTOR'S HANDBOOK: A MANUAL FOR SANITARY INSPECTORS AND OTHER PUBLIC HEALTH OFFICERS.—By Henry H. Clay, F.R.San.I., F.I.S.E., Major, R.A.M.C. Fifth Edition. 1942. H. K. Lewis and Company, Limited, London. Pp. xxii plus 534, with 97 illustrations. Price, 18s.

LIKE the earlier editions, this edition contains all the principal Health Acts which are pertinent to the duties of a sanitary inspector.

Some of the articles have been re-written, and valuable additions have been made.

More details could have been given on rapid and slow sand filtration, especially as to the quality and size of sand.

In chlorination no mention is made of the residual chlorine test.

Ventilation is well done, but the article on air conditioning is too brief, in view of the rapid multiplication of air conditioning installations, in the last few years.

The section on meat inspection is good, and the section on control of infectious diseases is better arranged than in previous editions, and also has some useful additions.

The book on the whole is very good and should be in every public health library.

B. R. D.

THE THEORY AND PRACTICE OF MASSAGE AND MEDICAL GYMNASTICS.—By Beatrice M. Goodall-Copestake. Sixth Edition. 1942. H. K. Lewis and Company, Limited, London (136, Gower Street, W.C.1). Pp. xx plus 370, with 129 illustrations (including 24 plates). Price, 16s.

MISS GOODALL-COPESTAKE has given us, in war time, a sixth edition of her book which was published originally during the last war. It is a book containing careful descriptions of all manipulations used for massage, and of their physiological effects. The chapters on muscle re-education are full, well arranged and easily followed. Exercises for medical and surgical conditions are carefully described with special emphasis on muscle work.

The volume is well illustrated. Special features of this edition are: an extension of the chapter on fibrositis and 'rheumatic' conditions; more information about congenital dislocation of hip and its treatment; a special chapter on war injuries, and the uses of plaster of Paris for immobilizing fractures. A bibliography gives titles of useful works on the subject of massage.

This book is one that can be used as a textbook for students, or as a reference book for those in practice.

P. B.

MEDICAL RESEARCH COUNCIL. SPECIAL REPORT SERIES NO. 235. 'THE CHEMICAL COMPOSITION OF FOODS.'—By R. A. McCance and E. M. Widdowson. Third Impression. 1942. Published by His Majesty's Stationery Office, London. Pp. 150. Price, 4s.

THIS is the third impression of a book which has already established a place as a standard reference book on dietetics. Practically no change has been made in the form of the book, but it has been revised considerably. It is one of the easiest books to use in the preparation of diets; both grammes and ounces are given. The foods of course are English foods and will not cover the practice of those who have to prepare Indian diets; nevertheless, with the help of some small Indian pamphlet, such as Health Bulletin No. 23, where values of Indian diets are given, there should be no difficulty in meeting all eventualities.

Abstracts from Reports

ANNUAL REPORT BY THE CURATOR OF THE LABORATORY OF THE ROYAL COLLEGE OF PHYSICIANS OF EDINBURGH, FOR THE YEAR 1941

THE Laboratory has now been over 50 years in existence. Despite the present adverse situation the research activities have been fully maintained. In addition, it now undertakes Government work for emergency hospitals and military services.

In the histology department, a special study of hæmatology was mainly directed to the establishment of different standards and simplified procedures. In the bacteriological section there was special work on *Trichomonas vaginalis* and *Oidium albicans*. The chemists have continued the work on synthesis of organic bases of possible anti-malarial or trypanocidal power.

Reports issued from the laboratory number 17,182, compared with 16,035 in 1940. There were eleven publications during the year.

Correspondence

PERIPHERAL NEURITIS

SIR,—In the editorial column of the January number of the *Indian Medical Gazette*, I note some interesting remarks on Naga sore sometimes having peripheral neuritis as its sequel.

I, as a tea garden practitioner, have to deal with a good number of these cases, but have never met peripheral neuritis in patients suffering from Naga sore. Local symptoms, pain, œdema and fever due to absorption of toxin are generally common.

The article has thrown new light as regards the causative organism of Naga sore. I and my many colleagues have treated these cases with various antiseptics and intravenous arsenic, believing the spirochæte to be the only causative organism, but without promising results. Failing in this line of treatment, I treated some of these cases by dusting with fine powder of magnesium sulphate and keeping the part bandaged and at rest, the idea of the application of magnesium sulphate being to increase the flow of lymph. This method, though rather painful, cured a good number of cases but some showed no marked improvement, so I began to use sulphanilamide (M.&B. 693 and streptocide) in the same manner as magnesium sulphate and got brilliant results, the cure being cent per cent.

Now, if the Klebs-Loeffler or diphtheroid organisms are one of the causes or associated organisms of Naga sore, then it seems possible that sulphanilamide has a bactericidal or bacteriostatic action on these organisms.

Malnutrition is marked in patients suffering from Naga sore. These patients generally belong to the lower status of the society. Peripheral neuritis may be an associated condition.

J. P. DEB, L.M.F.,
Assistant Medical Officer.

KUTTAL TEA ESTATE,
CACHAR, ASSAM,
P. O. SILCHER,
19th February, 1943.

SOME POSSIBLE NEW LINES OF TREATMENT OF SHOCK

SIR,—A new view of shock is given below which opens up a new line of treatment simple enough for any medical man to use. At the same time one cannot expect it to be used unless reasons are given for its use. I therefore give the pertinent facts and reasons, and, for brevity, give them dogmatically. Anyone, however, who wishes to go further into the facts can do so from the references given.

Our thinking machine, the brain, works on two sources of interacting energies almost as does the petrol motor, and these cerebral energies have been given the symbols H and L, respectively. H provides us with awareness and judging capacity, L provides the data for judging. The existence of these two sources of energy, it may be mentioned, is an automatic consequence of the colloidal structure of nerve cells (Burridge, 1932). In addition, the brain, like any other machine, has a limit to its normal functional capacity. This limit is denoted by the symbol, T, and the relations between H, L and T are given by the formula $H + L = T$ (Burridge, 1932, 1932a, 1933).

It will be seen at once that, because of T, the more there is of H, the less can there be of L, and *vice versa*. Such relationships between H and L have actually been appreciated ever since there were philosophers, but, as none previously realized they depended on T, an important factor making all the difference to the conclusions reached has so far been missing from the speculations.

If H be next regarded as analogous to air, L to petrol vapour and T to cylinder capacity, the petrol motor provides a useful and directly understandable

picture of the working of our own mental machinery. There is, however, the difference that the mental machine seems able to work on the thinnest and thickest of mixtures. Also of interest may be the fact that it can be supercharged either with H or with L. We then get fits, supercharging with H giving the hysterical and supercharging with L the epileptic type of fit (Burridge, 1933).

The phenomena of vision provides the simplest way to see the significance of the composition of the mixture in mental phenomena (Burridge, 1932a). Thus, staring intently at the black hat in the perfectly dark room demonstrates that H is ineffective to give a result without adequate L. Such phenomena have been termed *infra-cognoscible*.

In the next stage a little light is let into the room but not enough to see exactly what is there. One just realizes that an indefinite something is present. Such phenomena have been termed *hypophasic* (Burridge, 1932a, 1933).

When the illumination has been increased enough to show exactly what is there, the phenomena become *eucritical*, and I have used the term *eucritical* rather than Head's *epicritical* because I find the 'epi' misleading (Burridge, 1932a, 1933).

For the next three stages the hat is assumed to be replaced by a translucent globe containing a light of which the intensity can be gradually increased. The globe's illumination will be *eucritical* when we can see its outlines as definitely as those of the *eucritically* illuminated hat. But, if the illumination be increased beyond this, we gradually pass to the next stage, the *paracritical* stage, where we cease to see a globe but see something globular instead.

All other sensations will on examination be found to provide gradations similar to those just noted for light. When a man has *eucritical* toothache, for example, he knows exactly which tooth aches. But when the pain grows stronger, he so ceases to be able to judge exactly which tooth aches that he may direct the dentist's attention to the wrong tooth. It has not been previously recognized, however, that this 'spread' of pain is a phenomenon similar to the 'spread' of light.

The 'spread' which marks *paracritical* sensation is a direct consequence of our thinking machines having limited powers. In *paracritical* phenomena the energy which provides the data of the sensation has become so great as to preclude use by the thinking machine of enough of the other type of energy, that which gives judging capacity, to give accurate judgment. And while the incompatibility of much data with good judging capacity has not been previously recognized in relation to the simple sensations, it has always been recognized in relation to the more complex data-phenomena associated with what we call the passions. The factor T thus unifies a multitude of phenomena (Burridge, 1932a, 1933).

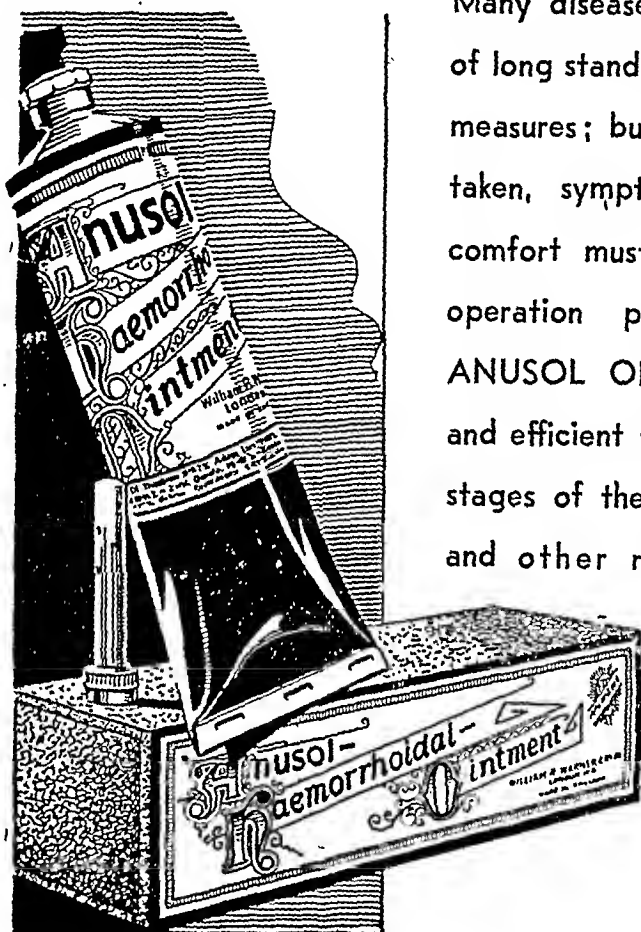
Paracritical pleasure may be exemplified by the sexual orgasm though this, when really good, probably belongs to the next stage of *ultra-critical* phenomena in which nothing matters except the sensation which is experienced, or the idea passing under review.

The site of origin of this pleasure is as limited as the site of origin of the pain of an aching tooth. It is noteworthy also that, if the current explanations of the spread of the pain of an aching tooth were valid, *viz.*, a breakdown of nerve insulation, spinal sclerosis would be the lot of all past their first youth; except, of course, for real virgins!

The data of sensation can surpass the *ultra-critical* and reach the stage of the *ultra-cognoscible* where cognizance is no longer possible. When the sensation is painful, shock results.

One result of the receipt of such 'sensations' is an apparent apathy. The individual's attention is so directed to a 'sensation' of which he cannot obtain cognizance that it would be as reasonable to expect him to pay ready attention to questions concerning his name, age, etc., as it would be to expect similar attention from one who is having a good tooth extracted without anaesthesia.

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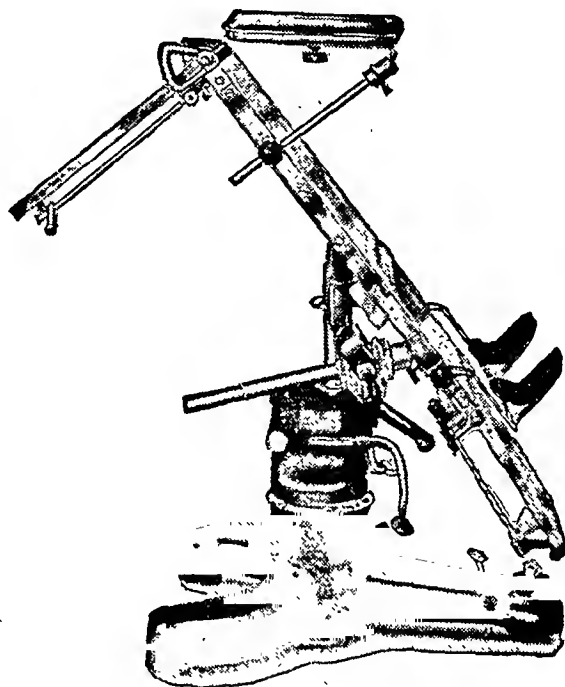
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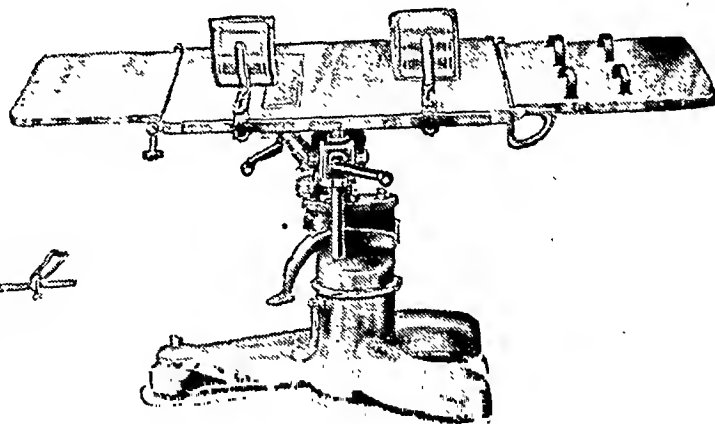
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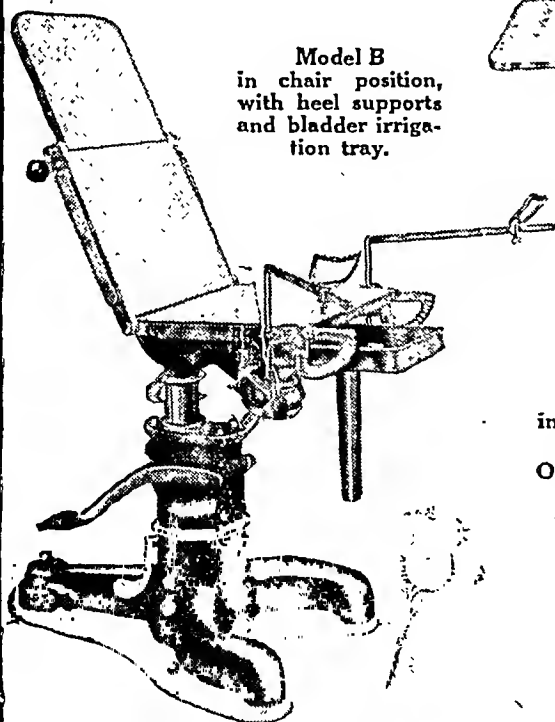
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and bladder irriga-
tion tray.

The ultra-cognoscible also implies that over-stimulation which effects decalcifying and inhibitory actions (Burridge, 1932). Over-dosing a heart with adrenaline, for example, regularly produces inhibition (Burridge, 1917). These large doses still stimulate, it should be noted, but the stimulation is swamped by decalcification and inhibition by potassium salts (Burridge, 1917, 1932). Something similar probably happens in shock. Calcium is not only the great antagonist of such over-stimulation, but also its natural and real antagonist (Burridge, 1932). Calcium is further essential to the functions of membranes, especially their permeabilities (Burridge, 1932).

To sum up, then, the fact that a shocked person no longer feels pain is not evidence that he is not receiving strong and nocuous stimulation from an injury. It should rather be regarded as the evidence that he is. If things be so then a seemingly obvious procedure would be to block all sensory nerves coming from an injured area so far as is possible. Spinal anaesthesia for anything 'below the belt' could thus well be routine. Some may see in this a local application of Crile's anoci-association, but there is the difference that we reach our conclusion through realizing that our brains, as thinking machines, have limited power.

Nothing that has been said above contraindicates the established lines of treatment commonly used, e.g. serum. At the same time, however, it should be appreciated that an excellent therapeutic agent may compensate the effects of shock rather than eradicate their cause. What is given above is believed to bring us nearer to eradication.

For purposes of co-ordination it may finally be noted that ultra-cognoscible phenomena would be termed 'repressed' by Freudians (Burridge, 1932a, 1933). They believe that consciousness represses or thrusts from itself such ideas or sensations whereas matters appear to be really just the other way about. It would appear, in fact, that those of old who concluded that emotion drives out awareness and reason were more correct than the modern Freudians. In addition, Freudians have mixed up ultra-cognoscible with infra-cognoscible phenomena (Burridge, 1932a, 1933).

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W. BURRIDGE, D.M.,
 M.A. (Oxon.),
 Professor of Physiology.

KING GEORGE'S MEDICAL
 COLLEGE, LUCKNOW,
 6th August, 1942.

[Note.—The manuscript reproduced above as a letter originally reached us on 11th August, 1942. It was not then published as an original article because the ideas advanced were not supported by experimental or clinical data, and the presentation seemed to be rather fanciful. Since then, an article on the treatment of shock has become available in the *British Medical Journal*, and is reprinted in our current topics section, page 218. This article, as does the above letter of Dr. Burridge, stresses the importance in the production of shock, of excessive stimulation of certain parts of the nervous system, and also advocates the intra-ventricular injection of potassium salts in the treatment of shock. The administration of potassium is not suggested by Dr. Burridge; he gives first place to the blockage of sensory nerves from the injured area.—
 EDITOR, I. M. G.]

Service Notes

APPOINTMENTS AND TRANSFERS

INDIAN LAND FORCES

(Emergency Commissions)

To be Major

Girdhari Lal Puri. Dated 9th January, 1943.

To be Captains

G. M. Mallesu. Dated 5th June, 1942.
 Badrud Din Ahmad. Dated 6th January, 1943.
 Suhas Kumar Roy. Dated 8th January, 1943.
 Ayodhya Nath Sinha. Dated 9th January, 1943.
 Pratul Chandra Mitter. Dated 17th January, 1943.
 Kaikhushru Bomanji Palkhivala. Dated 25th January, 1943.

20th September, 1942

John Gwesyn Davies. John Hlewellyn Edgar
 Thomas Jenkin Davies. Millen.
 George Arnold Flann. Clifford Vipon Oldroyd.
 John Elwyn Iias Hughes. Dudley Stuart Piper.
 Frederick Graham Millar. Hugh Chapman.

7th January, 1943

Satish Chandra Das. Bandla Venkiah Naidu.

8th January, 1943

Bimalananda Ghosh.
 Pramod Kumar Pannalal Trivedi.
 Prem Chandra Roy Asawarival.
 Radhicanranjan Chaudhuri. Dated 11th January, 1943.
 Bishnupada Mukopadhyaya. Dated 14th January, 1943.

(Within Indian Limits)

To be Captains

Ramaswamy Sundaram Iyer. Dated 6th January, 1943.

Beli Ram Abrol. Dated 8th January, 1943.

9th January, 1943

Harris Samuel Henry. Saifuddin Ahmad.
 Madho Swarup Gupta.

To be Lieutenants

John Michael Mungavin. Dated 21st February, 1942.
 James Grant Howie Davidson. Dated 6th November, 1942.

19th November, 1942

Jatindra Kumar Roy.
 Anil Behari Sen Gupta.
 Mandayam Annadhorai Narasimha Iyengar.
 Nitai Charan Ray.
 Anil Chandra Das Gupta.
 Kalyan Kumar Lahiri.
 Arabindra Chatterjee.
 Kumud Kanta Guha.
 Manmatha Bhusan Chakraborty.
 Pabitra Kumar Basu. Dated 25th November, 1942.
 Nakuleswar Sen. Dated 26th November, 1942.
 Santosh Kumar Muhury. Dated 26th November, 1942.

Hari Das Ghosal. Dated 27th November, 1942.

John Raj Samuel. Dated 4th December, 1942.

Harold William Charles Griffiths. Dated 6th December, 1942.

Maurice Philip McMurray. Dated 14th December, 1942.

William Stanley O'Malley. Dated 17th December, 1942.

Ray Maurice Burton Penhearow. Dated 19th December, 1942.

Edward Nelson Plomer. Dated 23rd December, 1942.

Harnam Dass Grover. Dated 8th January, 1943.

Ratnasami Gnanadorai. Dated 9th January, 1943.

Joseph John Denis Lobo. Dated 17th January, 1943.

7th January, 1943

Sekharipuram Venkataraya Sastri Krishnan.

Amirdasawmy Kanaga Raj.

Brij Nath Bhargava. Dated 9th January, 1943.

Bhavisetty Visweswa Rao. Dated 10th January, 1943.

Robert Henry Palmer Fitzpatrick. Dated 25th December, 1942.

8th January, 1943

Prabhakar Balwant Pandhey.

Binoy Bhushan Dutta.

Ram Narayan Banerjee.

Lok Nath Budhraj.

Kinavoor Kovilakth Udaya Varma Raja.

Sitaramasarma Kalyanasundaram.

Laxmi Narayan Ganti.

Harwood Raw Jacob.

Herbert Pushparaj Gaanaolivu.

9th January, 1943

Manickam Parkson Jesudasen.

Mark Francis D'Silva.

Narendra Nath Banerjee.

Allampally Ramachandracharya.

Thekkepat Karunakaran.

Bijjulla Padmanabha Reddy.

Thomas Sathya Das.

Khalifa M. N. Peer Mohamed.

Panchapikesan Krishnaswami.

Mundyath Janardhana Menon.

Pramendra Nath Bhattacharjee. Dated 11th January, 1943.

12th January, 1943

Valangaman Srinivasa Raghavachari.

Sevilimedu Krishnamachari Srinivasan.

Nadathur Narasimhan. Dated 15th January, 1943.

(Within Indian Limits)

To be Lieutenants

Sarup Chand Vij. Dated 11th November, 1942.

Abdul Hakim Khokhar. Dated 20th November, 1942.

To be Lieutenant for service in Royal Indian Navy.

Sundaresa Narayanan. Dated 9th January, 1943.

PROMOTION

INDIAN LAND FORCES

(Emergency Commissions)

Captains to be Majors

S. V. Velankar. Dated 23rd October, 1942.

Manuel Joseph Saldanha. Dated 23rd October, 1942.

Lieutenant to be Captain

H. Chapman. Dated 20th September, 1942.

C. Chandwani. Dated 27th September, 1942.

S. Hasan. Dated 7th November, 1942.

4th December, 1942

P. Deb.

P. Basu.

E. Bheemasankaran.

E. D. Anklesaria. Dated 8th October, 1942.

M. B. Thakore. Dated 18th October, 1942.

S. K. Rao. Dated 4th November, 1942.

6th November, 1942

I. R. Bazlicl. M. B. R. Khan.

G. S. Marathey. Dated 11th November, 1942.

2nd December, 1942

R. Roy. S. M. Ghosh.

B. Patra. Dated 4th December, 1942.

5th December, 1942

S. N. Mitra. K. C. Koshy.

S. Ghosh.

6th December, 1942

S. R. Paul. S. Somasundaram.

N. Prakash. A. K. Nambiar.

10th December, 1942

N. C. Talpatra. B. Ghosh.

P. K. Banerji. Dated 16th December, 1942.

4th January, 1943

M. L. Sudan. S. D. Sikand.

S. S. Muthanandam. Dated 22nd January, 1943.

A. David. Dated 2nd February, 1943.

A. Narasimham. Dated 5th February, 1943.

Lieutenants (on probation) to be Captains
(on probation)

J. M. R. M. Johnson. Dated 20th September, 1942.
1st January, 1943

S. C. Paul. N. N. Ghosh.
C. S. Balasubramaniam.

3rd February, 1943

S. D. Surie. S. B. S. B. Bhalla.

(Within Indian Limits)

Lieutenants to be Captains

I. Narayan. Dated 6th November, 1942.

S. K. Mozumdar. Dated 16th December, 1942.

R. Chandra. Dated 1st February, 1943.

RETIREMENTS

Colonel H. S. G. Haji, M.C. Dated 28th November, 1942.

Colonel P. B. Bharucha, D.S.O., O.B.E. Dated 21st February, 1943.

Lieutenant-Colonel B. R. Chaudhri. Dated 2nd December, 1942.

Lieutenant-Colonel S. D. Sondhi, M.C. Dated 14th January, 1943.

Major J. H. Boulton, on account of ill health.
Dated 26th September, 1942.

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Original Articles

THE PATHOGENESIS OF HEPATIC CIRRHOSIS

By A. S. JOHNSON, B.A., M.B., B.S., M.R.C.P. (Edin.)
Medical Wards of the District Hospital, Kottayam

THE striking frequency of the occurrence of hepatic cirrhosis and other liver diseases in the area round about Kottayam has for some time evoked the interest of doctors in this hospital. Dr. K. T. Kurian, my co-worker in the medical wards, has had occasion to note the diet of the people in three or four centres, and he has intimate knowledge of the habits and natural conditions of this northern part of Travancore. In the assessment and evaluation of the ætiological factors, therefore, his information and help have been found valuable.

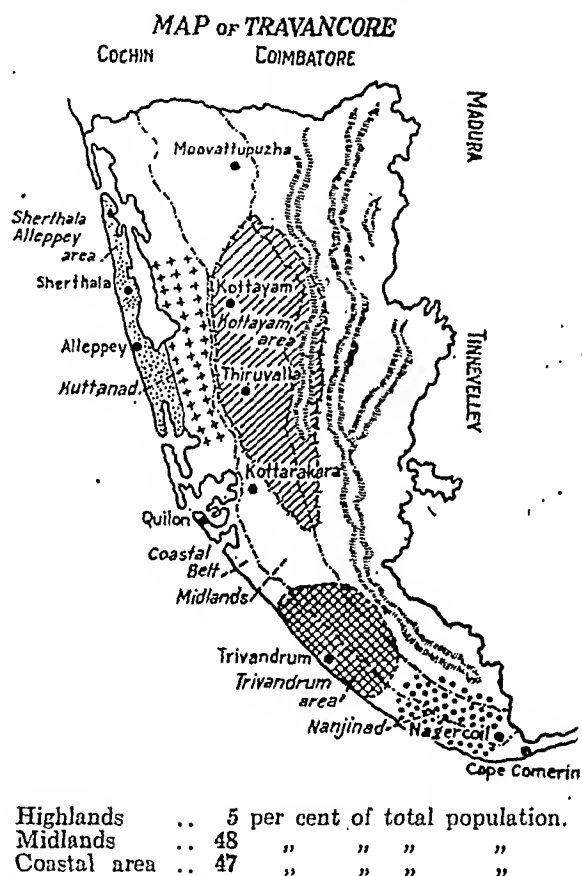
The distribution of cirrhosis, and diet.—Travancore can be divided into three areas, the coastal sandy belt, the midlands, and the highlands full of hills and forests. The coastal belt is divisible into two halves, one north of Quilon and the other south of Quilon, extending to the Cape. The northern part is full of backwaters, and is damp and sandy, but the southern part is comparatively dry and hilly. Further, in the northern half of the coastal belt between the extreme coast and the midlands is the marshy Kuttanad area where paddy is grown in large quantity. South of Quilon there is not much difference between the coastal area and the middle zone, since the land tapers to an angle towards Cape Comorin. Near the southern extremity is the Nanjinad area, famous here for the quality of rice produced.

Liver disease is more common round about Kottayam than round Trivandrum. The preponderance of hepatic cirrhosis also is noticed in the Kottayam area. Though amœbic abscess of the liver and hepatitis are frequently observed in the marshy Kuttanad area, it has to be admitted that cirrhosis of the liver is most common in the Kottayam area. Amœbic infection is common in both the areas under reference. Alcoholism also is common in these areas. What then is the factor that predisposes to a greater incidence of hepatic cirrhosis in the Kottayam area? A solution of this problem is likely to cast some light on some factors influencing the causation of liver cirrhosis.

In the *Trivandrum area*, rice is the staple food. Fish is available in all the parts round about. Fresh and leafy vegetables are also plentiful. Tapioca is available but it is not so intensely cultivated in this area as in the Kottayam area, and it is not so commonly used for food here as elsewhere. In the Nanjinad area (the coastal belt still further south of Trivandrum), tapioca plantations are few. This area is famous for the champa rice produced

from the extensive paddy-fields. In general this area is dry and healthy. Green and leafy vegetables can be had at all times, and fresh fish also is available. In this Nanjinad area, cirrhosis of the liver is less common than elsewhere in Travancore. In *Kuttanad* paddy is grown in plenty. Fresh fish, some vegetables and eggs are available for food. Here it is usually observed that rich men who take alcoholic liquors and develop pot-bellies are the people who suffer most from liver cirrhosis.

The *Kottayam area* is well in the interior away from the coast. Places in the interior are hilly and are used for the cultivation of tapioca, tubers, and starchy roots which are used for food in large quantities. Fresh fish is not available and limited salted fish is available.



Rice is used only to a limited extent in this area. Since the cultivation of tapioca requires little labour, practically no after-care and little initial expense, the ryots commonly grow this crop. Usually tapioca is cut into bits and dried as such. When used for daily consumption, the bits should be boiled first, and the water used for the purpose should be decanted to remove the toxic contents of the root. The tapioca so treated is less toxic. In the Kottayam area, hepatic cirrhosis is noticed to affect the stout and hardy labourers quite unlike the pot-bellied men of the better-fed classes affected in the Kuttanad area. These hardy labourers return home after daily toil to eat a meal prepared from dried tapioca and to drink a decoction made of coffee parings with no sugar. They

suffer not only from undernutrition but also from malnutrition.

It is profitable to compare these men with men who eat such toxic tapioca in the Sherthala-Alleppey area. Here fresh sea-fish such as sardines are available in abundance for food. Tender coconuts are also available in plenty, since in this area coconut palms are the common plantations. Thus vitamins and fats available in abundance compensate for the deficiencies in the staple food.

The above comparative study of diet in the various areas in question is representative of the whole of Travancore as pointed out in the map attached. The population in the highlands is only 5 per cent of the total population of Travancore. The Kottayam area where tapioca cultivation is maximum, the Trivandrum area, the Sherthala-Alleppey area on the extreme coast, the marshy Kuttanad area, and the Nanjinad area with the paddy cultivation cover almost the whole of the midlands and the coastal belt, which have a percentage population of 48 and 47 respectively.

The following suggestions are made:—

1. Toxins are present in the tapioca used as staple food.

2. Vitamin deficiencies are noticed in men using this common diet of the Kottayam area. Hepatic cirrhosis is also very common here. A combination of hepatic cirrhosis and vitamin deficiencies is also observed in cases here.

3. In some areas, though toxic tapioca is used by the people, cirrhosis of the liver is rarer than in the Kottayam area, since vitamin deficiencies are made up by other articles of food.

Toxic foods.—The ingestion of leaves of the tapioca plant, especially some varieties of these plants, results in the death of the cattle that take them. Children taking raw tapioca (any variety) feel giddy and vomit. It is known that cyanides are present in the plant and roots of the tapioca planted here. The poisonous effects are probably due to the cyanides. The Berlin blue reaction is found to be positive in the extracts from tapioca.

It has been observed in early cases here that a generalized flushing of the skin with indefinite and vague symptoms of weakness and languor, at times appearing like neurasthenia, formed the indications of the oncoming disease. In a patient aged 22, a sturdy hardworking young ryot taking tapioca as staple food, a generalized flush was followed by general anasarca. The anasarca responded to vitamin B₁ administered parenterally. His general condition became apparently normal. Three such cases have been observed here with no special reference to the liver. In the case of a boy of 10, a clear case of cirrhosis of the liver with some ascites, a generalized flush and vague feelings as described above were observed. He had night-blindness and dry skin. His ascites increased rapidly and he died 2 months after he came under observation. I think that a generalized

flush with vague nervous symptoms indicate the onset of the cirrhotic change in the liver. Some patients give a history of jaundice once or twice before manifest symptoms of cirrhosis of the liver had been noticed. Patients with cirrhosis become pale and anæmic, with a typical hepatic facies. The anæmia is evidently due to the embarrassed liver not functioning properly and giving a deficient supply of liver principle, and the pallor is due to the presence of a mild degree of jaundice in addition to the anæmia. The initial flush occurring in cases of hepatic cirrhosis may be due to the liver cells liberating histamine, as they are being subjected to the action of toxins. The flush is constant in progressive cases and in others it occurs periodically. Finally in advanced cases a pale pinched face with malar flush, at times, is left. The liver is a silent organ with a wide margin of safety. The symptoms of disease depend on the ultimate exhaustion of hepatic reserve. Vague pains and tenderness in right upper abdomen, or indigestion especially after heavy and fatty meals indicate that the liver is below par.

Vitamin deficiency.—The food consumed by the poor is so devoid of nutritive elements that the vitamin stores in the liver are exhausted. This is very marked in the tapioca consumers in Travancore. The toxins consumed day after day poison the liver cells, since liver is the major detoxicating organ. The polygonal cells are subjected to the influence of repeated action of mild doses of poison. The protective action of the vitamins against the toxins is not available. Further, toxins in their turn deplete the liver of any remaining vitamins. If the liver cells are bathed in glycogen, the effect of toxins will be minimized. Inadequate diet wanting in essential food factors, including vitamins, brings about exhaustion of the liver store, and over-work takes away any available glycogen in the liver cells. Toxic food material such as tapioca and coarse coffee ingested daily after hard labour pave the way for the exhaustion of the glycogen store in the liver cells, and devitalization and degeneration are found to follow in the unprotected cells.

In the Sherthala-Alleppey cases, it was pointed out that though the poisonous food factors are the same as in the Kottayam area, the simultaneous intake of adequate vitamins and fats prevents the development of cirrhotic changes in the liver. Some cases of hepatic cirrhosis improve after the administration of vitamins and fats others are refractile, probably because fibrosis has proceeded too far to permit of any regeneration taking place.

Vitamin A is a fat-soluble substance found in liver fat. About 95 per cent of the total body store of vitamin A is in the liver, the remainder being chiefly in the kidneys, lungs and suprarenals. When vitamin A is absent from the liver, it is also absent from other organs. The store is small in the newborn, and increases rapidly through the milk nutrition. In adult

animals, the liver store of vitamin A begins to increase within a few hours after the administration of a large dose of the vitamin; over 70 per cent of the quantity supplied may thus be stored.

Vitamin A deficiency is manifested by night blindness, and by excessive keratinization of the epithelium of skin and mucous membranes. Subnormal nocturnal vision responds to two weeks' administration of vitamin A. The more severe deficiency phenomena occur especially when the intake and absorption of the vitamin are decreased by prolonged gastro-intestinal disturbance. This observation may help us in reconciling Arthur Hurst's observations on alcoholic gastritis being the precursor of cirrhosis of the liver with the view taken in this article that vitamin A deficiency is one of the causes of cirrhosis. The polygonal cells of the liver become open to the action of toxins, being devoid of the help of glycogen and vitamins.

Liver changes.—The unit of the liver is a lobule. The Glisson's capsule is the fine areolar tissue covering the liver as a whole and extending into the liver substance through the portal fissure and surrounding the portal systems (a branch of the portal vein, a branch of the hepatic artery, and a bile duct). Each lobule is about 1 mm. in diameter and is separated from others by connective tissue. The Glisson's capsule is continuous with the connective tissue coat of the lobules. Under ordinary conditions, the areolar tissue coat of the lobules contains the fat. Of course the liver cells do contain some fat. The hepatic vein, which is centrally placed in the lobule, drains the blood brought by the portal vein and the hepatic artery. The toxic material conveyed in the portal blood stream initially affects the small portal systems, and hence the connective tissue around the lobules and later the peripheral part of the lobules. Probably the toxin destroys the vitamin A stored in the areolar fat, and irritates the connective tissue into overgrowth. The polygonal cells of the liver are affected next by the toxins, which cause them to succumb easily if their resistance is lowered by the depletion of vitamin A and glycogen. Vitamin A is stored in the liver fat. According to Muir the most effective liver poisons are fat-soluble substances such as phosphorus, tar, and sudan III. Naturally the fat-soluble poison conveyed in the portal blood is dissolved in the liver fat, and either destroys or displaces the vitamin A content, and irritates the connective tissue into overgrowth. Simultaneously the poison affects the liver parenchyma, also causing cellular degeneration and shrinkage and encouraging compensatory overgrowth of connective tissue.

Causes of cirrhosis.—What then is the toxin that is produced or absorbed from food? There must be some unity or similarity between the toxins that affect the cells. Hepatic cirrhosis is of world-wide distribution. Partly on the basis of aetiology, partly on the distribution of the

fibrous tissue and partly on age of incidence, many varieties of cirrhosis have been described. When once the exact nature of the lesion is understood, it is highly probable that the varieties spoken of will be recognized to be stages in the cirrhotic process. A fibrosis occurring in the liver, whether multilobular, unilobular, intercellular, pigmentary or biliary may have a common genesis. The toxins produced from or by the various food materials used in different places and suspected to be causative of liver cirrhosis probably have something in common.

Alcoholism has been said to be the cause of hepatic cirrhosis; in mental-hospital practice, cirrhosis of the liver is rare, though alcoholism is frequently noticed among the inmates. Alcoholism does not evidently produce cirrhotic changes in the liver either in its acute phase or in its chronic phase. Cirrhosis is probably the late manifestation of secret drinking, or excessive drinking leading either to nervous or cardiac symptoms. Liver disorder is no rarity in mental hospitals, but liver cirrhosis resulting from alcoholism is rare indeed. As Arthur Hurst thinks 'It is probable, therefore, that alcohol produces cirrhosis of the liver indirectly by leading to gastro-enteritis; the poisons produced in the stomach and intestines are absorbed and pass to the liver. As ordinary gastro-enteritis does not lead to cirrhosis, an additional factor must be present. This is probably the direct poisonous action of alcohol and occasionally of other toxins, such as that of malaria, on the liver cells, which thus become more liable to injury by gastro-intestinal toxæmia'. Only 5 to 6 per cent of alcoholics develop hepatic cirrhosis. The alcohol factor in the genesis of hepatic cirrhosis is not clear. Probably it is indirect. Any method of administration of alcohol in animals does not produce cirrhosis. Hunt found that long-continued administration of alcohol to guinea-pigs increases their susceptibility to the fatal action of acetonitrile. This is attributed to a derangement of metabolism which hastens the decomposition of the non-toxic nitrile into the cyanide. Further Litiner claimed that even small doses render the erythrocytes less resistant to hæmolysis and the organism less resistant to infection. Alcohol is less soluble in fats than in water. Therefore the toxic effect of alcohol on liver cells is likely to be slight. Fat-soluble toxins are more harmful to liver parenchyma than other toxins.

In the Kuttanad and other rice eating areas, hepatic cirrhosis, whenever it occurs, is noticed in the pot-bellied, overeating rich men who are alcoholics. Thus in the areas providing fairly nutritious food for the common folk, alcohol is found to devitalize and devitaminize the hepatic tissue and thus pave the way for cirrhosis. However rich and nutritious the food may be, its effect on the internal organs is reduced, since gastro-enteritis prevents proper absorption. The protective help of these factors, when toxic or infective agents affect the liver parenchyma, is

not available, and the cells have to bear the brunt and suffer the consequences. Another important point to note in the group of cases under consideration is the fact that rice is the staple food, and it provides a non-toxic variety of dextrose for the protection of the liver cells at least in the non-alcoholics.

Alcohol acts as a stimulant and activator of metabolism. It affects carbohydrate metabolism since, by the chemical energy liberated, alcohol can perfectly replace carbohydrates and fats in the diet. The primary increase in muscular work produced by a moderate dose of alcohol appears to be due directly to the food value. Thus alcohol takes the place of dextrose when used in moderate amount. In treatment of some nervous manifestations of alcoholism, the effect of glucose given intravenously was found to diminish the craving for drink. A patient aged 55 years, from Palai, showed alcohol deprivation symptoms. On the basis of treating morphinism with 25 per cent glucose (as advocated by Chopra and Chopra, 1937) I administered 25 c.cm. of 25 per cent glucose intravenously, daily, at the same time allowing alcohol to the patient. The dose of alcohol given was reduced gradually. In a couple of days the patient expressed an aversion from alcohol and was completely relieved of the symptoms. Incidentally this case may suggest a method of treating the alcohol habit.

Administration of small but repeated doses of insulin to normal subjects results in hypoglycæmic symptoms. Schizophrenics stand large doses of insulin, even 100 units, without manifestations of hypoglycæmia. I have been trying the effect of liver extracts (anahæmin, campolon, or erythgen) with the object of removing any resistance to insulin due to any torpidity of the liver in such cases. After the injection of liver extract, I have invariably found smaller doses of insulin producing hypoglycæmic symptoms. I have noticed that, as schizophrenic symptoms decreased in severity, the dose of insulin required for the shock to be produced and the need for the injection of liver extract became progressively less. From these observations it appears that there is some state of the liver which produces the mental symptom complex called schizophrenia, and that the efficiency of the liver function is gauged by the dose of insulin used.

In the case of a few confirmed hepatic cirrhosis patients treated with only 5 units of insulin each alarming symptoms of hypoglycæmia were noticed to develop, as anticipated. The symptoms subsided when properly treated. From these observations it becomes clear that the effective dose of insulin for the production of hypoglycæmic shock is determined by the proportion of healthy liver left. Thus it is possible to evolve an insulin test for the estimation of the glycogenic function of the liver.

The total glycogen content of all the muscles is, normally, about as great as that of the liver. Muscle glycogen may be mobilized to some extent

to help to maintain the blood sugar level. But the muscle glycogen is more slowly liberated into the blood stream than liver glycogen, for fatal hypo-glycæmia may occur in the presence of enough muscle glycogen to maintain the normal level of blood sugar for a considerable period. The liver in the diabetic is absolutely necessary for the production of hyperglycæmia, since the blood sugar of the diabetic is largely made in the liver and not from the muscle glycogen. Insulin causes the tissues to remove the sugar from the blood, and prevents the liver from forming fresh sugar from amino-acids. The onset of hypoglycæmia affects the central nervous system, and impulses pass out along the sympathetic nerves to the liver and to the adrenal medulla to mobilize liver glycogen and to retard the fall of blood sugar. If the liver is extirpated, there is no recovery of blood sugar after the injection of insulin. Thus it can be seen that the liver is necessary for the effects of hypoglycæmia to be removed, and that only liver glycogen is mobilized by insulin. Therefore a standardized insulin test should serve as a measure of the glycogen capacity of the liver.

On this basis I have found that the glycogen content of patients with cirrhotic livers is poor. This lack of glycogen is one of the causes of liver-cell damage.

According to McIndoe and Counseller, the division of the liver into two lobes by the antero-posterior fissure is incorrect; but the correct division is indicated by a line drawn from before backwards through the fundus of the gall-bladder to the spot where the inferior vena cava grooves the back of the liver. In splenic anæmia the left lobe of the liver is markedly affected, since the stomach and spleen are drained by the left lobe of the liver. In this case the poison producing fibrosis is most probably generated in the spleen and transmitted to the left lobe of the liver. Areas exposed to the toxins are first affected. If the spleen is removed early in splenic anæmia, cirrhosis of the liver does not occur.

In the hepato-lenticular degeneration of Kinnear Wilson, the pathogenesis of liver cirrhosis is not clear. If it were due to a lesion in the lenticular nucleus, the same type of cirrhotic change in the liver will be expected in Parkinson's syndrome resulting from encephalitis lethargica or otherwise. It has been suggested that manganese poisoning, which results in cirrhosis of the liver, may be compared to the cirrhosis associated with lenticular degeneration. The resemblance is said to be striking.

An irritation of the fibrous tissue resulting in cirrhosis of the liver is noticed in bronzed diabetes and other pigment cirrhosis. In malaria with acute hepatitis, and gastro-enteritis, the irritation of the hæmosiderin deposited in the peripheral cells of the hepatic lobules, and possibly poisons from the spleen, cause the hepatic cirrhosis.

Cases of infantile biliary cirrhosis, commonly met with, are found to occur in families, and further among the well-fed or rather over-fed children in India. Mukerji regarded it as a result of some virus infection conveyed in the mother's milk. Green-Armitage believes that deficiency of vitamins in the mother's diet depresses the mammary secretion and endocrine function of the fetus. The child is over-fed when born and the milch animals are insufficiently fed. Megaw has traced a close association between cirrhosis of the liver and bacillary dysentery. This has not been borne out in a study of cases examined here and elsewhere (at the General Hospital, Madras). Gibbons says that it is a peculiar form of biliary cirrhosis, the consequence of the action on the liver cells of some irritant of gastric origin which leads to a degeneration of the cells in the first instance, with subsequent increase of intercellular connective tissue and later of the portal sheaths. R. Rao calls it a subacute toxic cirrhosis. The varying degrees of necrosis of liver cells, the avascular oedematous connective tissue, and the obliterative lesions of the terminal and some of the bigger divisions of the hepatic venous tree without appreciable changes in the portal and biliary trees are clearly pointed out as the outstanding features in the liver in cases of infantile cirrhosis. There is a poor attempt at regeneration of the hepatic parenchyma (Manson-Bahr, 1940.)

In support of Green-Armitage's view, the following case can be quoted. Twins, a girl and a boy, 11 months of age had an unequal start and entry into the world. The girl was smaller than her twin brother, due to unfavourable intra-uterine conditions. Four months after birth the girl suddenly increased in weight and became twice the size of her twin brother. At the age of 7 months, evident cirrhotic changes had developed in the child. A good supply of milk and vitamins improved the child's state.

The view that hot curries and highly seasoned food help to cause hepatic cirrhosis cannot be taken too seriously. Considering the large proportion of the population using this type of food, the incidence of hepatic cirrhosis is rare, and infants never take highly seasoned or hot food.

From the groups of cases referred to above, it is seen that hepatic cirrhosis can occur in people who have never touched alcohol in any form. It is found to affect men and women in India where some communities abstain from the use of alcohol in any form. J. S. Young is reported to have tried sudan III along with sodium cholate in varying doses. 'The lesions of acute and sub-acute atrophy, multinodular hyperplasia and cirrhosis' can be produced under such conditions. 'Each of these changes may follow the injection of a single dose.' This indicates the possibility that cirrhosis of the human liver may follow damage inflicted at any one time. Cameron has suggested that newly formed connective tissue may undergo absorption at a later stage, and dis-

appear. The ætiological factors appear to be many, but the pathological manifestation in the form of one reaction, namely fibrosis, indicates a common mode of attack on the liver cells. Even in malarial cirrhosis, the antecedent condition is found to be gastro-enteritis. Either gastro-enteritis or food deficient in vitamins prevent the liver from obtaining vitamins A and B, and pave the way for the onset of hepatic fibrosis. It is quite possible that normal metabolism may be disordered, and, instead of the production of the usual non-toxic metabolites, abnormal products toxic in their reaction may be produced. Under normal conditions when the bile canaliculi are patent, liver parenchyma regenerates to the extent of about 70 per cent of the normal, even if toxic products cause necrosis in the cells. But if biliary obstruction is present in any degree, as is likely in gastro-enteritis, necrosis is likely to progress. Thus in biliary as well as other types of cirrhosis, the fibrosis is primarily connected with a devitalizing food causing gastro-enteritis, disordered metabolism, faulty absorption and hence a poor supply of essential food factors such as vitamin A to the internal organs. The toxic metabolites act on the liver parenchyma, and with the low vitamin A content and a low glycogen content of the liver cells, hepatic degeneration sets in, and irritative or compensatory overgrowth of connective tissue results. In this process, the obstruction of biliary canaliculi by an extension of the catarrhal changes of the alimentary tract is bound to help by preventing regeneration.

Summary and conclusions

A general analysis of the habits and food used in the Kuttanad, Sherthala-Alleppey, Kottayam, Trivandrum, and Nanjinad areas is made. The use of poisonous tapioca is considered to cause severe damage to liver tissue, due to lack of adequate vitamins and other food factors. The similarity of effect on the liver resulting from other causes is dealt with. The rôle of vitamin A and the effect of other food factors are also considered. A possibility of the assessment of the glycogenic function of the liver by standardized insulin administration is suggested. The importance of early diagnosis of the condition before the lesions are too far gone is stressed.

In treating liver cirrhosis, the use of alcohol and alcoholic drugs should be prohibited. The stomach of cirrhotics should be washed and gastro-enteritis attended to. Vitamins are not absorbed when given orally. Therefore parenteral therapy of liver extracts, vitamins A and B and glucose has to be resorted to. Milk diet with some eggs must be used in such cases. Dr. Krishnan working in the Coonoor Laboratories under Dr. Aykroyd has found that Travancore children living on tapioca alone improved in weight and general health when milk in some form was added to their diet. The deficiencies of a tapioca diet are made up by the milk fat

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THE TAKATA-ARA TEST

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and

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CLAIMS have been made from time to time about the value of the Takata-Ara reaction as a test for cirrhosis of the liver. As galactose is not easily available at present, we decided to do this test instead of the galactose-tolerance test to ascertain the functional efficiency of the liver. As a preliminary measure we carried out the test in various diseases with or without clinical manifestations of hepatic dysfunction, to determine its real diagnostic value.

History

In 1925, Takata introduced a laboratory test for the differentiation of lobar from broncho-pneumonia. In the same year Takata and Ara using cerebro-spinal fluid, reported further experience in the test which suggested its use in differentiating between meningitis and syphilitic involvement of the central nervous system. These

(Continued from previous page)

and vitamins. An early diagnosis of the liver affection, and an adequate supply of vitamin and other food factors, supplemented by an attempt at the removal of the toxic effects of poisonous food material (tapioca cyanides), are essential prerequisites for a successful treatment. The methods of detoxication and the effect of particular lines of treatment on selected types of cases are under investigation.

This investigation of hepatic cirrhosis was taken up in the medical wards here at the initiative of Dr. Jacob Taliat, district medical officer and officer in charge, District Hospital, Kottayam. This article is the result of his inspiring influence and encouragement.

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investigators attributed the flocculation in the positive Takata-Ara reaction to a change in the albumin-globulin ratio in the serum or spinal fluid.

In 1924, Adler and Strauss found that hepatic damage alters the relationship of the serum albumin and globulin.

Having these facts in mind, Staub in 1929 suggested the utilization of the Takata-Ara test as a diagnostic measure for liver diseases. He found the test positive in all cases with severe parenchymatous liver damage.

Jezler performed the test on serum and ascitic fluid, and reported positive results in cases of severe parenchymatous disease of the liver, especially cirrhosis.

Since then numerous investigations have been reported in the literature concerning the various aspects of the reaction. Many investigators have obtained positive results in a large proportion of cirrhosis cases; Kirk in 1936 collected from the literature 375 cases of liver cirrhosis, of which 315 gave a positive reaction. Earlier reports seemed to suggest that the test was specific for hepatic cirrhosis. More recent reports show that the reaction is by no means a specific one for cirrhosis.

Method

We performed the tests according to the following method except in a few cases at the beginning; in these basic fuchsin was added and 8 tubes were used as originally suggested. Since the precipitate and not the colour changes are important, we later omitted the fuchsin solution. Further, as a precipitate in the last 2 of the 8 tubes is not significant, we used 6 tubes only for each test.

One cubic centimetre of 0.9 per cent sodium chloride solution is put into each of six small test-tubes. To the first tube, one cubic centimetre of clear serum to be tested is added and the contents are thoroughly mixed. One cubic centimetre of this mixture is removed and added to the second tube and the contents are thoroughly mixed. Next one cubic centimetre is transferred from the second to the third tube and the contents are thoroughly mixed. The process is repeated in the remaining tubes, the one cubic centimetre from the sixth tube being discarded. The dilutions of the serum are 1:2, 1:4, 1:8, 1:16, 1:32, and 1:64. To each of the tubes is added 0.25 c.cm. of 10 per cent solution sodium carbonate, and 0.15 c.cm. of 0.5 per cent mercuric chloride solution. The mixtures are shaken and then allowed to stand at room temperature overnight, and the readings are made next day, when tubes showing a definite precipitate are noted.

Interpretation

There seems to be a lack of uniformity with regard to the criteria for reading this test. According to Heath and King, the reactions showing complete precipitation in 1 tube or some flocculation in 5 tubes were considered strongly positive; those showing almost complete precipitation in 1 tube or flocculation in 3 tubes were considered positive. Slight but definite flocculation in 1 or 2 tubes is considered weakly positive. Those showing no flocculent precipitation are negative.

Some workers interpret the results as follows :—

- +++ a definite flocculation in 4 or more tubes or in 3 tubes at least 1 of which shows a flocculation occupying about one-third of the column.
- ++ a definite but small flocculation in 3 or 4 tubes.
- + a definite but minimal flocculation in more than 3 tubes.
- ve all others.

Halfstrom reads the results as follows :—

Slight turbidity	+
Incipient flocculation	++
Clear flocculation	+++
Maximum flocculation	++++

According to Bray, a definite precipitate in 2 of the first 3 tubes is positive. In positive reactions, the precipitate may occur also in tubes 4, 5 and 6. Negative reactions show no precipitate in any tubes, or a slight precipitate in tubes 4, 5 and 6.

Following Bray, we interpreted our results as follows :—

- Strongly positive—definite precipitate in all tubes.
- Positive—definite precipitate in 2 of the first 3 (usually a precipitate also occurs in tubes 4, 5 and 6).
- Doubtful positive—definite precipitate in one of the first 3 tubes, as well as in the last 3 tubes (4, 5 and 6).

As a rule, an initial precipitate was produced in each tube; hence the readings taken soon after the test is performed are all positive. Obviously this reading is of no value. The twenty-four-hour reading was most constant, and this was noted, particular attention being paid to flocculent precipitation. Simple clouding or haziness, or even a doubtful precipitate in any tube was disregarded. Occasionally, there was a brick-red precipitate; this coloration was considered

to be of no significance. Sometimes, there was a heavy precipitate at the bottom of the tubes; this however, on shaking, appeared to be of a flocculent character.

Mechanism of the Takata-Ara reaction

The formation of the flocculent precipitate depends upon an alteration in the protein constituents of the serum. Some investigators believe that the factor of primary importance is the lowered albumin content. The albumin fraction normally is said to exert a protective action, thus preventing the flocculation of the colloidal solution of mercuric oxide formed by the interaction of mercuric chloride with sodium carbonate in the presence of proteins. Others take the view that the increased globulin content is the responsible agent. The Takata-Ara test is apt to be positive in any condition in which the serum globulin is raised.

It has also been stated that as a result of hepatic dysfunction, abnormal metabolic products circulate in the blood and give rise to the positive reaction. Such products are said to include proteins which are liberated from the dying or dead liver cells, and which are brought to the liver but are not adequately dealt with.

The reaction has been attributed to various other factors also, *viz*, disturbance of ammonia level in the blood, increased H-ion concentration, certain fatty acids, diminished heparin, alteration of tryptophane content, etc.

Results

Our series includes Takata-Ara tests performed 129 times on 120 persons. The following tables are a summary of the results obtained :—

Diagnosis	Number examined	TAKATA-ARA REACTION			
		Strongly positive	Positive	Doubtful reaction	Negative
Liver diseases—					
Cirrhosis	6	..	1	1	4
Malignant	4	..	2	..	2
Jaundice	3	1	2
Hydatid	1	1
TOTAL	14	3 (21.4%)	2 (14.3%)	9 (64.3%)
Kala-azar before treatment ..	44	19 (43.2%)	16 (36.4%)	5 (11.4%)	4 (9.0%)
Kala-azar after treatment ..	20	5 (25.0%)	4 (20.0%)	11 (55.0%)
Splenomegaly	19	1 (5.3%)	1 (5.3%)	17 (89.4%)
Other conditions	32	1 ..	31 (96.9%)

Details of other conditions

Tuberculosis ..	5	Nephritis ..	1
Malaria ..	4	Septic tonsils ..	1
Enteric ..	3	Asthma ..	1
Leukæmia ..	2	Cerebral tumour ..	1
Anæmia ..	2	Dermal leishmaniasis ..	1
Gastric ulcer ..	1	Ariboflavinosis ..	1
Diarrhoea ..	1	Debility ..	1
Dysentery ..	1	Normal ..	5
Gall stones ..	1		

Only one case of malaria gave a doubtful reaction, the rest were all negative.

The Takata-Ara test in a series of 9 kala-azar cases before and after treatment

Before		After	
1	Negative	Negative	
2	Strongly positive	Positive	
3	Positive	Negative	
4	Strongly positive	Positive	
5	Doubtful	Doubtful	
6	Strongly positive	Negative	
7	Positive	Positive	
8	Positive	Negative	
9	Strongly positive	Doubtful	
Positive ..		Positive ..	3
Doubtful ..		Doubtful ..	2
Negative ..		Negative ..	4

Summary

The Takata-Ara test was performed on 120 persons. These included 14 cases of hepatic disorder, 55 of kala-azar, 19 of splenomegaly, 27 of heterogenous conditions, and 5 normal persons.

In a series of untreated kala-azar patients, about 80 per cent gave a positive reaction, while only 25 per cent were positive just after the treatment. Out of the 14 cases with definite involvement of the liver, only 3, i.e., 21.4 per cent, were positive. Ninety per cent of the non-kala-azar splenomegaly cases were negative. None of the miscellaneous group gave a positive reaction.

Conclusions

The Takata-Ara test cannot be regarded as a specific test for cirrhosis of the liver. It is frequently positive in kala-azar. In kala-azar the euglobulin is constantly found increased. Therefore it appears probable that increase of euglobulin in the blood, which may of course be due to liver damage, is the determining factor in causing a positive reaction.

Acknowledgment

This work was undertaken at the suggestion of Dr. L. Everard Napier, Director and Professor of Tropical Medicine, Calcutta. Our thanks are due to him for allowing us to do the tests on patients under his care at the Carmichael Hospital for Tropical Diseases, and for his valuable advice and guidance.

DETERIORATION OF ASCARIDOL IN OIL OF CHENOPODIUM

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BEFORE the advent of carbon tetrachloride and tetrachlorethylene, oil of chenopodium was largely used in the treatment of hookworm infection all over the world. Though the oil was made official in the U.S.A. Pharmacopœia long ago, it was not until 1932 that it found its place in the British Pharmacopœia. According to the Pharmacopœias of both the countries, the oil should contain not less than 65 per cent w/w of ascaridol, and should be kept protected from light and stored in a cool place.

It has been known for a long time that the percentage of ascaridol varies in different brands of the oil. Caius and Mhaskar (1920) found the ascaridol content to be 60, 62 and 70 per cent in three different samples of the oil. They also quote that Schimmel and Company found ascaridol in proportions varying from 45 to 65 per cent in different samples. That ascaridol deteriorates by storage was also noted by Caius and Mhaskar (*loc. cit.*).

They estimated the percentage of ascaridol in an indirect way. Measured quantities of the oil were dissolved in 90 per cent alcohol and shaken vigorously with a saturated solution of ferrous sulphate. A violent reaction ensued with the evolution of much gas and a rise of temperature. The reduction of the oil was considered to be complete when gas production ceased and no further rise of temperature occurred on further addition of ferrous sulphate. In this way they found that from 60 to 70 per cent of the oil was reduced, the amount varying in different samples. The portion of the oil which had not reacted was separated and this oil called by them 'residue oil' had no anthelmintic value. They thus considered that reduction was confined to the ascaridol fraction which carries the anthelmintic property of the oil, and they used this as a method of estimating the amount of ascaridol.

By this indirect method of estimation, in two samples of the oil they found that the ascaridol content (60 per cent) of one sample was not diminished after eighteen months, but, in the other sample, it had fallen from 70 to 66 per cent in seventeen months, with changes in physical constants also.

This appears to be the only instance where the oil was tested for ascaridol (though indirectly) after a period of storage.

Now that during the war, tetrachlorethylene is almost out of the local market, one of us (A. K. M.) decided to treat a series of cases of helminthic infections with oil of chenopodium. An original phial of the oil which had been lying in our department in a steel cupboard for two years was opened, and the ascaridol content tested by the standard B.P. method of assay proved

to be only 49.16 per cent. This oil, when manufactured, had probably not less than 65 per cent of ascaridol, as it was labelled 'Oleum Chenopodii B.P.', but we had no means of knowing either the date of manufacture or the amount of deterioration in the two years. We, therefore, decided to study the actual progressive deterioration of ascaridol in oil of chenopodium kept in and away from light. We took out from our stock another original phial of the oil of a different maker. This oil was purchased recently and was kept in a steel cupboard. In February 1941, we divided the contents of the phial into four smaller bottles, two brown and two white. We kept one brown and one white bottle in the laboratory in a glass cupboard and the similar other two inside a steel cupboard (sample 1). Another bottle of a different maker was purchased in March 1941; its ascaridol content was tested, and it was stored under the same conditions (sample 2).

We began testing the ascaridol content periodically from March 1941. All the estimations were done by the same worker (B. K. G.) by the standard B.P. method of assay, partly in the Biochemical Standardization Laboratory, Calcutta, and partly in the chemistry department of our School. We believe that the personal factor of error has thus been reduced to a minimum. The percentage of ascaridol is shown in the following table :—

	KEPT IN DARK		KEPT IN LIGHT	
	Brown phial	White phial	Brown phial	White phial
SAMPLE 1				
March 1941	65.44	63.8	64.9	64.2
June 1941	60.7	58.7	61.3	57.1
March 1942	53.8	54.0	55.8	54.5
January 1943	52.6	53.1	55.2	54.0
SAMPLE 2				
March 1941	70.1	70.1	70.1	70.1
June 1941	62.6	65.2	69.3	67.1
March 1942	60.6	59.3	Used up for clinical trial	62.1
January 1943	56.3	52.8	Do.	55.1

It will be seen that there is a progressive deterioration of ascaridol in both the samples whether kept in dark or in light. The deterioration is more rapid during the first year than subsequently. The room temperature during these experiments varied between 98°F. and 70°F.

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A PRELIMINARY NOTE ON THE PREPARATION OF SEITZ FILTER-PADS IN THE LABORATORY

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ASBESTOS filter-pads for use in the Seitz filter for the purpose of obtaining sterile filtrate from any contaminated fluid have been successfully prepared in our laboratory by using a special grade of asbestos generally known as asbestos wool, and cellulose pulp.

Preparation of cellulose pulp

The cellulose pulp is made by soaking in water overnight coarse filter-paper or ordinary blotting paper, and then kneading the whole mass by hand. The coarse pulp is strained in an ordinary linen bag, remixed with a large volume of fresh water, and boiled for half an hour. During the time of boiling, the pulp is stirred briskly. After cooling to room temperature, the water is strained off and the pulp is mixed with a fresh quantity of water and churned in a hand milk-churn till the pulp appears homogeneous. The water is then removed through filter-paper in a Buchner funnel by means of a water-suction pump. When all the water is sucked out, the pulp appears as a thick paper pad. It is washed again with distilled water in the same Buchner funnel. The paper pad is then taken out and dried in a hot air oven at 100°C. The pure cellulose pulp thus obtained may be kept for future use in a dry place away from dust particles.

Preparation of asbestos pulp

Asbestos wool of best quality obtained from The Asbestos Belting Co., Ltd., Calcutta, is made into pulp by cutting small tufts of asbestos wool with a pair of scissors into the smallest bits possible. Such a procedure is essential for preparation of good asbestos pulp. The best pulp is made by means of a pulping machine. For want of proper equipment, pulp grading was not possible; nevertheless by cutting with a pair of scissors, good workable pulp could be made.

The finely-cut asbestos wool is washed three times with a large volume of 0.5 per cent hydrochloric acid in freshly made distilled water in a thoroughly cleaned vessel, preferably a glass one. After each washing, the water is sucked out of the pulp through a lint cloth in a Buchner funnel. Here again in the Buchner funnel is produced a pad, which is freed from any trace of acid by repeatedly washing with distilled water by means of water-suction pump. This asbestos pad is then dried in a hot air oven at 100°C. The purified asbestos pulp in the form

of a pad is also kept in a dry and dust-proof vessel for future use.

The asbestos pulp and cellulose pulp being ready, we can prepare the final filtering-pad at any time we require it.

Preparation of filtering-pads

Filtering-pads are made by mixing, in a hand milk-churn, asbestos and cellulose pulp in freshly made distilled water, and casting the thoroughly mixed pulp in a Buchner funnel lined with lint cloth cut to the size of the funnel. The proportions of the two pulps and the amount needed are given below. The water is removed from the pulp mixture by means of suction. A small quantity of the mixed pulp sufficient to fill two-thirds of the funnel is poured over the lint cloth fixed in the funnel by previously soaking it with water. The funnel is then rocked horizontally in all directions for some time in order to distribute and 'felt' the fibres uniformly. When all the water is sucked off, leaving a dry thin layer of pulp over the lint cloth, another portion of the mixed pulp is poured over the previous one, cautiously so as not to break the layer already formed. This is best done by placing a strip of paper about 3 inches wide over the previous layer and pouring the liquid pulp over the strip of paper. The paper is drawn out of the funnel immediately after the pouring of the pulp is finished. The funnel is again rocked horizontally several times to distribute the pulp uniformly. This procedure is repeated as each layer dries up, till the whole pulp is used up. After the final layer is set, the pad is washed by sucking absolute alcohol through it three times in small quantities. This procedure prevents subsequent turbidity in the filtrate. The final pad is then taken out of the funnel, pressed as tightly as possible between two wooden blocks faced with filter-paper, and allowed to dry in the hot air oven at 100°C. The dry pad should be kept in a dry and dust-proof box for future use.

The proportion and amount of asbestos and cellulose pulp and water used in making pads of 6 cm. diameter is as follows :—

Dry asbestos pulp	..	3 gm.
Dry cellulose pulp	..	6 gm.
Distilled water	..	1,000 c.cm.

The amount needed for pads of other sizes can be calculated.

If finely-cut asbestos pulp is available, the proportion of asbestos can be reduced, and that of cellulose pulp increased. In this case the total weight and the thickness of the pad can also be reduced. With ungraded asbestos pulp, it is possible to prepare pads giving uniform results only by making them thick. Standard foreign pads of 6 cm. diameter weigh about 3 gm. each, but our pads being prepared from ungraded and roughly made pulp weighed about 9 gm. each. Thirty batches of pads, 6 cm. in diameter, were

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A CASE OF ENLARGED THYMUS GLAND

By M. V. BHAJEKAR, M.A., M.B., F.R.C.S.

and

S. G. TALWALKAR, M.B., D.A.R.C.S.

YOUNG AND TURNBULL (1931), in their analysis from a large number of cases, consider that an abnormally large thymus gland in itself cannot be considered to be indicative of status thymico-lymphaticus when no obvious cause of death is found at post mortem. On the other hand, Monerieff (1938) has remarked that an enlarged thymus is not a common chance finding in the chests of infants who have been x-rayed for other conditions, of heart or lungs. Also a study of a number of healthy infants attending a welfare centre has failed to reveal thymic enlargement similar to that seen in cases described by him, in which the symptoms were those of stridor, syncope and dyspnoea.

It appears clear however that a thymus gland which can be classed as abnormally big from an x-ray picture is not necessarily associated with symptoms. The following case is of interest in this connection :—

On 30th December, 1941, evening, while the mother was lifting her baby, a needle, which was tucked in the mother's blouse, pricked the baby's skin near the left nipple. As the baby kept on crying, and the needle could not be found, the mother concluded that the needle had probably remained in the baby's skin. On the

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prepared and tested. Each batch consisted of four pads, and all were found satisfactory.

The organisms detailed below were grown separately in nutrient broth and a quantity of about 100 c.cm. of fresh young culture of each organism was filtered through sterilized pads. The filtrates of different cultures were found sterile after incubation for four days at 37°C.

The organisms tested were :—

Vibrio cholera, *Bacterium typhosum*, *Chromobacterium prodigiosum*, *Pseudomonas pyocyanea*.

Ordinary tap water incubated with 1 per cent peptone at pH 7.4 overnight showed turbidity. This was also used.

As *Chromobacterium prodigiosum* is not retained by many old filter-pads, this organism is used as a standard for testing the usefulness of a filtering-pad. It is to be hoped that firms will take up the preparation of asbestos filter-pads according to the methods described and will thereby remove the keenly felt want in this war emergency period.

Note.—Two pads were tested by Dr. Ghosal at the All-India Institute of Hygiene, Calcutta, and three were tested by Major-General Taylor at the Central Research Institute, Kasauli. The latter reported that, compared with imported commercial filter-pads, these pads were thicker and softer, but the rate of filtration and the volume of filtrate were satisfactory, and the filtrate was sterile. The tests were made at pressures up to 10 lbs.

following evening, i.e. the 31st, this male Chinese seven months, old baby was brought to one of us (M. V. B.) with the above history.

On examination, the baby looked quite healthy though a little flabby, and on careful inquiry no history could be obtained of anything else wrong with the baby. On the skin, at the suspected spot, there was a small fresh puncture mark. A radiogram was taken with the intention of localizing exactly the situation of the needle. Dr. M. D. Joshi took the *x*-ray picture and reported as follows : 'X-ray shows two pieces of needle in the upper part of the abdominal wall on the left side. Thymus is greatly enlarged'. Immediately the question arose whether such a baby could be submitted to an operation for removal of the needle pieces, which would necessarily involve the administration of a general anæsthetic, and might take a long time to complete. With the consent of the baby's parents it was decided to operate.

On 1st January, 1942, one of us (M. V. B.) did the operation while the other (S. G. T.) carefully induced anæsthesia. One of the two needle pieces was easily and quickly removed. The second piece could not be found even after 10 minutes' search. The wound was therefore sutured, and it was decided to take another radiogram. This second *x*-ray picture showed the remaining piece just a little above the site of the incision.

On the following day, general anæsthesia was again induced, and the original wound opened. After 20 minutes of fruitless search a portable *x*-ray apparatus was brought to the theatre. This revealed that the piece was under one of the ribs, inside the thorax, and not just under the skin as previously supposed. A straight suture needle was then introduced until it came in contact with the needle piece. A mosquito artery forceps was passed along this needle and fortunately the needle piece was easily and successfully removed. The whole operation took 40 minutes, requiring a continuous anæsthesia of 30 minutes. Ten days later, the sutures were removed and the wound healed by primary intention. During the administration of the anæsthetic, a peculiar sound—thudd—was heard on auscultation, just below the sternal notch, at the end of each expiration.

The following precautions were taken before and during anæsthesia :—

1. Injection of atropine sulphate gr. 1/150 $\frac{1}{2}$ hour before administration of the anæsthetic.
2. Very gradual induction of ether anæsthesia by the open ether drop method.

3. Meticulous care to maintain a free and clear airway, and the administration of 300 c.cm. of oxygen per minute to avoid sub-oxygenation.

21st February, 1943.—The child who is now 18 months old was examined to-day and is found to be in good health. No unusual symptoms have developed during the year—there are no signs of stridor, dyspnoea or syncope. On auscultation, that peculiar sound—thudd—at the

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A RARE CONGENITAL ANOMALY PRODUCING A CLINICAL SYNDROME IN AN ADULT

By M. N. DE, M.B., M.R.C.P. (Lond.)

Professor of Medicine, Medical College, Calcutta

J. C. D., aged 46 years, a Bengali Hindu, had been suffering from periodic attacks of biliousness which, of late, had been so severe that he had to suspend his professional work. The patient, who was an intelligent and educated man, described his symptoms accurately. He stated that he had been 'bilious' from his childhood, but his first attack of serious bilious vomiting occurred in 1916. The next severe attack was in 1933, when it continued for nearly ten days. He kept well for some time, but his troubles returned, and the attacks continued intermittently for months. He consulted his doctors who suspected 'stomach trouble' for which a barium meal examination of the gastro-intestinal tract was suggested. A duodenal ulcer having been reported, the patient undertook a full course of Sippy treatment in a hospital. After this he kept well for a couple of months, but the same condition returned and, having found no relief, the patient came to Calcutta for diagnosis and treatment.

The attacks, as described by the patient, were of a uniform nature. They started early in the morning with a feeling of weakness and a peculiar sensation in the throat. This was soon followed by repeated bouts of vomiting of bile-stained material. He felt dizzy and lethargic, yawned frequently and was very weak. During this time his appetite was poor. He also suffered from a peculiar fear that he would not survive the attack. Previously the bouts used to last

(Continued from previous column)

end of each expiration is not audible. On taking a radiogram, the thymus appears to be definitely smaller than before, compared with the width of the thorax.

Holmes and Ruggles (1941) in their book on röntgen interpretation (page 172) say that 'in an enlarged thymus the shadow is more or less rectangular and overlies that of the upper border of the heart and great vessels'. The *x*-ray picture (plate XI) is typical of such an enlargement. The radiogram also shows the two pieces of the needle.

We must thank the Superintendent, Sir J. J. Hospital, for allowing us to publish the case, and Dr. M. D. Joshi for repeating the *x*-ray pictures.

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from three to four days, but their duration had since increased to about one week.

In the past, the patient had suffered from a serious attack of 'blood dysentery' in 1933 and had two severe mental shocks. He bled very badly when his teeth were extracted. His wife stated that he had lost much weight. He had never suffered from any pain in his stomach or abdomen. His appetite and digestion were quite satisfactory except during the attacks. He had always been constipated, but his stools were of good colour and consistency.

On examination, no abnormality could be detected anywhere except that many of his teeth were missing, and there was some tenderness in his left iliac region. All clinical and laboratory examinations were inconclusive.

A barium meal examination of the gastro-intestinal tract revealed a very interesting feature. The stomach was found to be perfectly normal. The first abnormality was found in the disposition of the duodenum. The cap was normal and there was no evidence of ulcer niche, crater, filling-defect or pressure-tenderness. The third part of the duodenum ran to the right, instead of to the left as in normal cases (see figure 1, plate XI); otherwise no abnormality could be seen. The last part of the duodenum was situated on the right side of the second part (not on the left as normally) and then crossed the latter to form the duodeno-jejunal flexure just below the base of the cap. All the jejunal coils were seen to lie in the right half of the abdomen below the liver instead of on the left. The cæcum was seen to be on the left side of the abdomen opposite the body of the third lumbar vertebra and about 2 inches to the left of the midspinal line, with the ascending colon running up towards the right across the vertebral column to the under surface of the liver, where it formed the hepatic flexure (see figure 2, plate XI). The transverse and descending colon were normally situated.

It will be seen from the above description that the patient was not suffering from any organic disease of the stomach or duodenum. There was definite radiological evidence of a developmental anomaly in the midgut, namely, (1) incomplete rotation of the large gut with the cæcum lying in the left half of the abdomen, and the ascending colon crossing the spine from left to right, (2) the jejunal and upper ileal coils lying in the right half of the abdominal cavity, and (3) the fourth part of the duodenum crossing the second part from the right to the left. One can only speculate on the cause of the patient's complaints, but the above developmental abnormality may have some connection with it. The last part of the duodenum, while crossing the second part, may cause, under certain circumstances, some compression on the latter, resulting in regurgitation of bile into the stomach, and precipitating the periodical attacks of bilious vomiting from which the patient suffered. The possibility of

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REGIONAL ENTERO-COLITIS (CROHN'S DISEASE)* †

By S. D. ARAWATTIGI

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In the recent literature of gastro-enterology, a disease of the small and large intestines has been widely recognized in America and Europe. Different designations have been used, such as regional ileitis, ileitis-terminalis, regional enteritis, non-specific granuloma, inflammatory tumour of the small intestine, chronic cicatrizing enteritis, localized hypertrophic enteritis, localized chronic ulcerative ileitis, and 'Crohn's disease'. It is surprising to note that so far the disease has not been mentioned in Indian medical literature, and no reference has been made to such a disease existing in Indians or in the foreigners residing in India.

About four years ago, the possibility of the occurrence of this disease in India was brought to my notice by a member of our staff. After a careful study of each case of intestinal affection, it was noticed that some cases, originally diagnosed as tuberculosis of the cæcum or of the abdomen, did not show any definite evidence of tuberculosis of the intestine or any other part of the body. Crohn's disease and tuberculosis sometimes show a similar clinical picture. During the past four years, my own cases of granulomatous intestinal lesion without tuberculosis have numbered twenty-six; and this does not include similar cases treated by other members of the staff in the hospital. It seems that the time has come to bring this subject forward for the consideration of others.

This disease was described by surgeons half a century ago; but in 1932 Crohn, Ginzberg and Oppenheimer of New York gave a clear idea of the clinical signs and symptoms of the disease, under the name 'regional ileitis'. Since then many cases have been reported by different physicians and surgeons in the United States of America and in Europe.

Various reasons exist for the diversity of the names used for this condition. The majority of writers are now using the terms 'regional ileitis'

* Paper read at the General Conference of the Christian Medical Association of India held at Miraj in December 1940.

† See editorial in this number.

(Continued from previous column)

an abnormal mesenteric vessel under such a developmental defect exerting pressure on the duodenum and causing its partial occlusion and leading to periodic bouts of bilious vomiting may also have to be kept in mind.

I express my indebtedness to Dr. B. N. Sinha, M.B., for bringing the patient to me and to Dr. P. B. Mukherji, for the radiological examinations, and also for supplying two negative prints.

or 'regional enteritis'. The latter name is preferred, since recently cases have been reported of jejunal involvement either separately or together with the ileum. Crohn and Rosenak in 1936 stated that colonic involvement never occurred; later on, however, they reported nine cases of ileitis with colitis. Some workers observed that, in cases of severe diffuse ulcerative colitis as well as in cases of localized right-sided colitis, a retrograde extension may occur in the ileum. My observations have included some cases with lesions in the cæcum and the ascending colon as well as in the ileum. The disease is therefore not particularly confined to the small or the large intestine, but it may involve both. Therefore I prefer the name 'regional entero-colitis'.

In *ætiology*, all attempts to isolate a causative agent have so far failed. Sections, cultures and animal inoculations have all been negative for tuberculosis. As to bacillary dysentery, Crohn found only one positive agglutination test for dysentery in his series. On the other hand, in 1936 Felsen and Gorenberg believed that they had traced eleven acute and eleven chronic cases of distal ileitis due to bacillary dysentery. Absorption of toxins and infection due to stagnation have been suggested as aetiological factors. In the majority of my cases, Lane's bands, adhesions round the ileum after appendicitis, producing partial obstruction with resulting hypertrophy and chronic irritation, were invariably detected. Such pathological bands may act as a predisposing factor. Amœbiasis is known to produce granulomatous lesions, and in a large number of my cases *Entamœba histolytica* have been isolated from the stools. It may be mentioned that in the experience of other workers, amœbiasis has never been observed.

The pathological study of the gross and microscopic features indicates that the disease may involve any part of the small intestine or the right side of the colon, including the mesenteric lymph glands. Usually the terminal ileum is the part most involved. The lesion at different parts of the gut is different. The ileum shows a granuloma, while the colon shows ulcerative and hyperplastic inflammation. The lesion is characterized by a subacute or chronic cicatrizing inflammation of all the coats of small or large intestine, forming a granulomatous mass in the abdomen.

In acute and subacute cases, the terminal ileum appears thickened, œdematous and acutely inflamed. There may be free fluid in the peritoneal cavity. The early pathologic findings are those of an acute inflammatory process of all coats of the terminal ileum. The appendix itself does not show any pathological change. Ulcerative areas may form on the mucosa. *B. coli* and non-hæmolytic streptococci are found in these ulcers. Exudation and hyperplastic reaction are especially marked in the submucosa, causing enormous thickening of the wall, producing a 'soggy' tube with a lumen perhaps so narrow that it will barely admit

a probe. An extension of the inflammatory changes is seen in the mesenteric lymphatics. These inflammatory changes progress to stages of resolution and repair until fibroblastic proliferation and scar tissue replace normal structure. Various stages of inflammation and repair are seen in the same specimen. Sections of lymph nodes show giant cells, and occasionally large pale cells, lying singly or in large groups, which are considered to be vegetable in nature. These are not characteristic features of the pathologic process, but may serve to intensify the process of fibrosis. Similar findings may be made in tuberculosis. One of the specimens removed at operation in this series showed linear scars across the serous coat of the intestine towards the mesentery, but no scarring on the anti-mesenteric border. In some specimens, perforation on the mesenteric side of the intestine takes place, with the formation of an abscess or fistulæ.

Age and sex.—This disease is confined to the young, usually under the age of 30 years. Females are more prone to this disease than males. In my series of 26 cases, 21 were females and 5 males. All were between 20 and 30 years, except two, of whom one was 35 and the other 36 years of age.

Symptoms.—The most outstanding subjective symptoms are pain, diarrhœa, continuous loss of weight and strength, progressive anæmia, nausea and vomiting.

Four types of cases may be generally recognized by their clinical symptoms. They correspond to the different stages of the disease.

Stage 1.—This is that type which simulates mild or acute appendicitis. On opening the abdomen, the appendix does not seem abnormal, but the terminal ileum or some other part of the intestine is found to be œdematous and red, and the adjacent lymph nodes are enlarged and inflamed. The mesentery is also œdematous. Occasionally perforation may be found to take place, with the formation of an abscess or peritonitis. Such a condition was well illustrated by a patient who was admitted to the hospital with definite signs and symptoms of acute peritonitis.

The patient, a female, 24 years old, stated that acute pain and tenderness of the abdomen came on suddenly three days before admission. On immediate laparotomy, a perforation, of moderate size, of the cæcum was discovered. Inflammation of the walls of the cæcum and the mesentery was marked. The regional nodes were moderately enlarged. The appendix and the other parts of the intestine were normal. Except cæcitis, no other lesion was detected pertaining to this disease. The perforation was successfully sutured and recovery was uneventful.

Another patient illustrates a different clinical picture seen in this stage. The symptoms were less marked.

A female, 25 years old, came to the clinic with the chief complaints of sterility and associated symptoms of retroversion of the uterus. On careful physical examination, a thickened tender intestine could be palpated. A history of a mild attack of pain in that area about a month before, and inability to extend

the right thigh for a few days were elicited. It was suspected that she had had an attack of *mild acute appendicitis*. An operation was advised for *insufflation of tubes*, correction of retroversion of the uterus, and appendicectomy. On opening the abdomen, a typical subacute inflammatory thickened terminal ileum was revealed. As usual, the mesentery was *oedematous with prominent and enlarged nodes*. A very large Meckel's diverticulum was found away from the lesion (see figure, plate XI). The whole affected part, including the cæcum, the mesentery and the enlarged glands, was successfully resected, and an end to end anastomosis was made. The necessary correction of the uterus was also undertaken. The patient made an *uneventful recovery*.

Stage 2.—These are cases which simulate ulcerative colitis. The patient has colicky pain, passing mucus, pus and blood in the stools, secondary anæmia, loss of weight and a constant low-grade fever. These cases are rarely seen by surgeons, but are often treated by physicians as either chronic dysentery or ulcerative colitis. When long continued treatment fails, they may be seen by a surgeon.

Stage 3.—Most patients are seen in this stage. These patients have intestinal obstruction of a chronic nature with cramping pain and a palpable mass in the right lower quadrant or the pelvis. These cases are usually diagnosed and operated on as tuberculosis of the cæcum. Twenty-three of my twenty-seven cases belonged to this group. All came with a history of chronic intestinal obstruction with a definite mass in the right iliac region. Another interesting manifestation of this disease is that it spreads, and spreads extensively. Crohn stated 'the disease acts as if it were an infection'. The case described below shows how the disease can spread rapidly and extensively within a short period.

A female patient, 28 years old, had an appendicectomy elsewhere in 1934. Four years later she came complaining of symptoms of partial intestinal obstruction, general emaciation, and anæmia, with a mass in the right lower quadrant; but no fever or cough. All the tests for tuberculosis were negative. Laparotomy was advised to relieve the obstruction. On opening the abdomen, a granulomatous mass was found involving the cæcum and the terminal ileum about one foot from the ileo-cæcal valve. As her general condition was not satisfactory, a lateral anastomosis between the proximal loop of the ileum about 2 inches above the involved area and the transverse colon was performed as a preliminary to resection. Her general condition showed a marked improvement. Twenty days later, when the abdomen was opened for resection, I found to my surprise that the disease had extended up along the ileum about 6 inches above the anastomosis. A drastic step had to be taken in view of the rapid spread of the disease in such a short time. Radical resection was done including the old stoma and the recently involved lesion. The improvement in her general condition was rapid and uninterrupted. She gave birth to a healthy child three years later. She does not manifest any signs of the disease.

Stage 4.—These cases show persistent intestinal fistulæ, and are usually neglected cases. The fistulæ may develop into the internal organs, such as the bladder, rectum or vagina, or point as an abscess which may rupture outside. Many such fistulæ will form in an old operation scar if the disease has been left unrecognized.

A patient, an emaciated individual, 25 years old, had occasional pain in the abdomen. Many days later, he developed an abscess over the right lumbar region. The abscess was incised, but the wound kept on discharging pus, with sinus formation. Every possible anti-tuberculosis treatment was tried, but nothing seemed to improve the condition. At this stage he came to us for treatment. During the course of his stay here, many attempts were made to close the sinus. On one occasion a trace of faecal matter was seen coming through the sinus. On the diagnosis of faecal fistula, the abdomen was opened, when a thickened and a chronically inflamed cæcum covered by dense adhesions was seen. The appendix was normal but a perforation was detected high up in the wall of the cæcum, which was covered with granulation tissue. As the closure of the sinus seemed difficult, the terminal ileum was divided and anastomosed with the transverse colon, in order to divert the faecal matter. Although there was slight improvement in the general condition, the patient developed another discharging sinus in the operation scar. A few days later, a complete resection of the divided ileum, of the thickened cæcum including the appendix and of half of the transverse colon was undertaken as the only method of cure. In spite of some local infection the wound healed and the fistulæ closed. The patient was discharged in good health.

Another case in stage 4 was in a male patient, 31 years old, who had been operated on elsewhere for pain in the abdomen in 1933. The operation then performed was ilco-colostomy. He was admitted to this hospital in September 1940 with a complaint of discharging sinus in the right iliac region. The history was that an abscess appeared in that area about six months previously and that it had been incised and operated on three times. The sinus persisted with no response to ordinary treatment. A diagnosis of intestinal tuberculosis was made, and for one year adequate general medical and surgical treatment was given. Though the general condition became very satisfactory, the sinus failed to close. No faecal discharge was detected. Laparotomy was advised, and it was discovered that the sinus communicated with the cæcum, which revealed extensive hypertrophic changes of all the coats, with many ulcers in the mucous membrane. The ileo-cæcal valve was almost closed. The terminal ileum also showed the same changes, and was much dilated. The mesentery was very much thickened, and contained many enlarged glands. The old stoma was detected and whole of the terminal ileum and the right half of colon was resected. The patient was discharged in December 1940.

Roentgenogram findings.—Dilatation of the proximal loop and Kantor's (1934) 'string sign' are well seen.

Diagnosis.—It may not be possible to diagnose acute cases before opening the abdomen. A mass in the right lower quadrant, emaciation, a scar of the previous appendicectomy, occasionally evidence of fistula, signs of chronic intestinal obstruction and Kantor's sign are valuable findings in chronic cases.

Differential diagnosis: *acute or subacute cases.*—A palpable mass is very rarely noticed in mild attacks of appendicitis but is fairly common in regional ileitis. Typhoid with perforation may be mistaken for a perforation due to regional ileitis. The laboratory findings will be valuable. In *chronic cases*, ulcerative colitis may be excluded by finding a mass in the right lower quadrant. Vomiting and other obstruction symptoms are not observed in simple ulcerative colitis. Perforation in colitis has not been observed by Crohn and Berg (1938) but a case of perforation of the cæcum with

right-sided colitis was seen in the present series. This is a very important finding.

Ileo-cæcal tuberculosis and regional ileitis present a similar clinical picture. The following points must be borne in mind in the differential diagnosis. Tuberculosis causes extensive involvement of the small intestine. Multiple tuberculomata are detected throughout the small intestine. In tuberculosis, small lesions are situated more towards anti-mesenteric border, while in regional ileitis, the mesenteric border is involved first. General mesenteric adenitis is observed in tuberculosis, while only the regional glands are involved in regional ileitis. Of course tubercle bacilli are absent from the stools.

Tuberculous lymph nodes become calcified, lose their 'bean-shaped' appearance and become spherical, while the natural shape is retained in regional ileitis even though they are enlarged.

Malignant diseases of the ileo-cæcal region such as lympho-sarcoma, Hodgkin's disease and carcinoma may cause confusion, but biopsy usually decides the question. Actinomycosis must be excluded when fistulæ are present.

Treatment.—The medical treatment is purely palliative, and it consists of nutritious diet of high vitamin content, and, in cases simulating colitis, retention enemas of neutral acriflavine of 1 to 4,000. When high titre agglutination of dysentery organisms is found, the injection of polyvalent anti-dysenteric serum is advised. Mercurochrome injections, anti-spasmodics and intestinal disinfectants have also been suggested. Repeated blood transfusions are valuable in building up the general condition.

The only method of cure is surgical. Various procedures have been advocated. *Ileo-colostomy*, lateral or 'end-to-lateral' has been done. When the lesion is confined to the terminal ileum, the end-to-lateral operation is preferable. This is reserved for incurable cases and does not prevent further spread of disease. *Ileo-sigmoidostomy* is done with the purpose of diverting the faecal stream from the right side of the colon. This and the previous measure are to be adopted for patients too weak to stand a radical resection which is the operation of choice. *Radical resection* has been accepted and is the only proper treatment available at the present time. Mixer (1935) points out that operation is often made difficult by hæmorrhage, thickened mesentery and complicating fistulæ. He reports a mortality of 36 per cent. Berg reports 32 cases done with only one death. When fistulæ are present, it is advisable to do the operation in two stages. Karl and Mayer think that the state of the mesentery may be an indication as to when to resect, when to short-circuit, and when to leave alone. The type of operation advocated by Berg is a wide resection of the diseased tissues of the ileum together with the cæcum and the ascending colon. An anastomosis between the ileum and transverse colon is established. The extent of the resection of the ileum is determined by the degree of mesenteric adenopathy.

The technique employed for these resections was that of Pemberton and Whittaker (1937) who report a mortality of two in a series of thirty-eight cases. Spinal anæsthesia, with its few disadvantages, I consider to be the anæsthetic of choice for the operation. Of the twenty-seven cases collected in the course of four years, twenty-six were successfully operated on by a one- or two-stage operation. There was only one death. The condition of this patient was so poor that he was kept in the hospital for 62 days, and an effort was made to build up his general health before the operation was undertaken. Another death was recorded six months after operation, when the patient developed obstructive symptoms. The obstruction was released by lateral anastomosis. Later, the patient developed two faecal fistulæ at the original wound and also severe cystitis, and *B. coli* septicæmia, and died.

Summary

Crohn's disease is prevalent in India. In view of its wide distribution in the ileum and colon, the designation 'regional enterocolitis' is preferred. It is observed that the disease spreads extensively and rapidly like an infection. Lane's bands, adhesions round the ileum and amœbiasis may be predisposing factors. Fistulæ may be due to perforation in the acute stage and not necessarily during the chronic stage. Radical resection is the operation of choice.

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THE MENINGIOMAS OF THE LESSER WING OF THE SPHENOID

By G. J. VAN DER HOEVE
and
J. KIJNE

DIAGNOSTICALLY as well as therapeutically, meningiomas of the so-called sphenoidal ridge present several difficulties. We therefore make a few remarks concerning the diagnostic aspects of this problem. In another paper we hope to deal with the operative treatment.

In a female patient recently seen, after long deliberation, we established a diagnosis of a meningioma of the innermost part of the sphenoidal ridge. This sphenoidal ridge can be divided into three almost equal parts, namely, the inner or clinoidal part, the middle or alary part and the outer or pterional part. In our case we had to deal with an affection having its seat in the inner or clinoidal part.

The case was in a Chinese woman, 46 years old, who, a year ago, came to the ophthalmologist with complaints regarding the left eye; the vision was at that time 1/6. She returned a year later with vision 1/60. There existed then on the left side a retrobulbar neuritis with a central scotoma, primary atrophy of the optic nerve, and complete ophthalmoplegia, while in the right side there was papilloedema.

An examination of the nasal cavities showed no irregularities. The left eye was slightly prominent. Neurologically no anomalies could be found; perhaps the strength of the left arm was slightly less than that of the right.

The patient complained of headaches, dizziness, pains in the left shoulder, sometimes also in the left arm. No pressure symptoms could be detected.

The eye symptoms, primary atrophy of the optic nerve on one side and papilloedema on the other, were first described in combination by Forster-Kennedy, who brought these eye symptoms into relation with irregularities of the frontal lobe.

It appeared later, however, that the Forster-Kennedy syndrome also occurred with meningiomas of the olfactory groove and also with meningiomas of the sphenoidal ridge.

The x-ray picture showed some peculiar features, but before I describe them, I want first to picture the different changes that may occur with lesions of this sort.

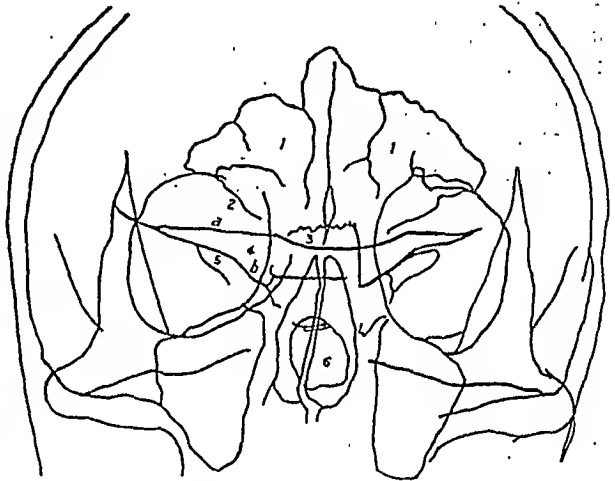
We will first consider the general changes in the skull and later the local changes caused by these tumours as shown in the roentgenogram together with the calcification that may result from such affections.

General changes.—Like every slow developing tumour of the brain, the meningiomas may cause secondary changes in the cranial bones, such as digitate impressions, broadening of the diploe, changes in the sella turcica, and modifications of the sutures of the cranium. As all of these symptoms are the results of a heightened

intracranial pressure, they are of no value in localization.

In addition to the classic changes, a massive and generalized thickening of the bone is often found at the wing of the sphenoid or at some other place. This change however is not specific for the meningiomas of the lesser wing, as it also occurs with gliomas and even during the development of an arachnoiditis, and is a reaction of the cranial bones towards a slowly developing process that induces a growing intracranial pressure. As we have said, just as with the other skull bones, a thickening of the lesser wing sometimes occurs, and as we shall see later, this thickening is occasionally asymmetrical, and this fact may lead to errors in the interpretation of the roentgenogram.

Local changes.—These are caused in various ways; pressure of invasion by the tumour, osteogenic reactions, thinning of the bone with



The normal x-ray picture.

1. Frontal sinus.
2. Supraorbital recess.
3. Planum sphenoidale.
4. Lesser wing of sphenoid.
5. Sphenoidal fissure.
6. Sphenoidal sinus.
- a. Upper border } Lesser wing of sphenoid (4).
- b. Lower border }

hyper-vascularization. These changes tend to be localized on the lesser wing, in the pterion, and near the sella turcica.

Local changes of the lesser wing.—These are manifold and varied. They may be unilateral or bilateral, and consist of decalcification and destruction of the bone, while on the other hand osteomas may occur.

Erosions of the lesser wing.—(a) General decalcification may affect the greater wing, and the whole structure of the orbit becomes hazy and uniform. Sometimes the fissures are scarcely distinguishable, and the upper margin of the lesser wing may be even more hazy.

(b) Local decalcification or true erosions are caused by the actual invasion of the tumour.

Bilateral erosions.—These are of no value in localization, as they may be found in any



Fig. 1.—Abnormally placed duodenum.



Fig. 2.—Partial non-rotation of the large intestine. Caecum seen on the left side. All the coils of the jejunum and ileum seen on the right side.

A CASE OF ENLARGED THYMUS GLANDS :
BHAJEKAR & TALWALKAR (PAGE 236)

REGIONAL ENTERO-COLITIS :
S. D. ARAWATTIGI (PAGE 238)



Skiagram showing enlarged thymus and two pieces of the needle.



Figure showing affected ileum and Meckel's diverticulum, and enlarged lymph nodes.

PLATE XII
THE MENINGIOMAS OF THE LESSER WING OF THE SPHENOID : G. J. VAN DER HOEVE AND
J. KIJNE



Fig. 1.—Homolateral erosion of the entire lesser wing.



Fig. 2.—The lesser wing seen as an irregular interrupted line.



Fig. 3.—Tumour at a distance. Erosion of the lesser wing.



Fig. 4.—Hyperostosis of the affected site.

case with high intracranial pressure. Bilateral erosions are sometimes caused by the tumour itself, sometimes by high intracranial pressure.

Unilateral erosions.—In these cases there exists a definite asymmetry of the lesser wing (plate XII, figure 1). Sometimes no detail is distinguishable in the orbit, which is totally hazy. When however the bone absorption is more localized, the lesser wing is visible only as an irregular line, interrupted in places (plate XII, figure 2). As a rule this decalcification is accompanied by haziness of the fissures; the contours of these flatten out, especially in the upper part. It is however not only the tumours of the upper cranial ridge that cause such changes.

According to Mayer, the tumours of the middle cranial fossa cause erosions of the lesser wing, especially at the posterior margin, while in cases of tumour of the anterior cranial fossa, changes occur in the anterior margin. Meningiomas of the lesser wing may sometimes be accompanied by erosions of the posterior margin, and sometimes of the anterior margin. In other words, the meningiomas of the lesser wing sometimes behave as tumours of the anterior fossa, and sometimes as tumours of the medial cranial fossa; this is easily understood, as they are located just at the border between these two cranial fossæ.

The unilateral erosion sometimes happens to be on the same side as the tumour, sometimes at the contralateral side. That means that the meningiomas are not invariably confined to the site of the visible changes. When one realizes that such changes may result from numerous causes, one appreciates the difficulties of interpretation of the roentgenogram.

Now what is the conclusion to be drawn from a roentgenogram such as that shown in figure 1 (plate XII) showing erosion of the lesser wing on one side and a normal condition on the other?

First it has to be understood that these irregularities have little diagnostic value for they may be encountered with quite a number of conditions, for example syphilis.

The following three groups of conditions have to be considered :—

1. Meningiomas of the lesser wing.
2. Tumours in the surrounding areas.
3. Heightened intracranial pressure.

With meningiomas of the lesser wing the erosion occurs on the affected as well as on the healthy side.

Homolateral erosion most frequently occurs as the result of local high pressure, or of a tumour eroding the bone.

Contralateral erosion is an important phenomenon, since it may lead to mistakes in the localization of the tumour. In most cases this contralateral erosion is the result of an unilateral expansion of the ventricles on the healthy side, compensatory for the reduced capacity of the ventricle on the affected side.

Tumours of the surrounding area, particularly meningiomas of the *tuberculum sellæ* and the

olfactory triangle, which is between the anterior and middle cranial fossæ, may cause a condition similar to the one described.

The lesser wing may become so thin that finally it feels like parchment. One also meets this erosion sometimes with tumours of the hypophysis. In all these conditions, differentiation may be difficult or impossible. If the lesser wing is being eroded by a metastatic tumour, the results are different. The lesions are not restricted to the lesser wing, and sometimes result in an extensive destruction of the bone, and that in a much shorter time than is usual with meningiomas.

With tumours at a distance and with raised intracranial pressure, very rarely is the lesser wing eroded on one side only; in exceptional cases this has been observed with tumours of the fourth ventricle, but they remain exceptions. Such a condition is shown in figure 3 (plate XII).

From the above discussion one may conclude, that unilateral erosion of the lesser wing is of some value in localization.

To summarize we may say :

1. The unilateral erosion of the lesser wing points to the existence of a tumour in the temporal fossa, but it leaves one in the dark about the character and site of this tumour.

2. Sometimes the unilateral erosion is caused by raised intracranial pressure, but if so it is usually accompanied by other symptoms of raised pressure.

3. In some cases of tumour of the middle cranial fossa, an erosion is found on the contralateral side, caused by ventricular dilatation.

All these changes, which separately have no value in localization, suddenly recover their diagnostic value, if they can be connected with other irregularities, such as peri-sphenoidal deposits of calcium, osteomas or other such conditions.

Hyperostosis of the lesser wing.—This is fairly common and is always situated at the same side as the tumour. These hyperostoses may spread over the whole wing, or may remain of a more local character.

Generalized hyperostosis usually appears as an osteoma of the lesser wing, and the diagnostic value is then great. As a rule, it is limited to the lesser wing, but there are cases in which the osteoma also affects the surrounding area. Cushing, Sosman, Putman and Mayer have given descriptions of cases where the lateral part of the orbit had been forced away by the osteoma. Generally the osteoma is located above and in front of the anterior clinoid process, having the form of an irregular triangle. To get a true impression of the extent and situation of the lesion, a stereophotograph has to be used.

Localized hyperostosis is always difficult to interpret in the roentgenogram. However if it is present, it always occurs on the side of the meningioma. In some cases, on the side of the tumour the lesser wing may be partly eroded,

while in addition a hyperostosis may occur on the same side (plate XII, figure 4).

Changes in the surroundings of the pterion.—The region of the pterion is a very important area. In the immediate surroundings, the lesser wing joins the lateral cranial bone; the middle meningeal artery here comes out of the bony canal, and the parieto-sphenoidal sinus suddenly changes its direction.

Affections of this area often occur in the so-called outer meningiomas. Cushing pointed out that the so-called meningiomas 'en plaque' show a marked tendency to produce exostoses here. With meningiomas of the lesser wing, the bony canal of the middle meningeal artery is often dilated on the affected side. According to Liebmman, Heuener and Dandy, this dilatation also occurs with quite a number of other tumours, and also in the course of development of an arachnoiditis it is no rare phenomenon.

Changes of the sella turcica.—These are very frequent. Bilateral and symmetrical changes of the sella possess no diagnostic value. They are the result of raised intracranial pressure. The unilateral irregularities of the sella have a much greater significance in the diagnosis of the meningiomas. The anterior and posterior clinoid processes on the healthy side show no anomalies. On the side of the affection, the contours of the sella are hazy. The anterior clinoid process looks ragged and is displaced upwards. The fossa is dilated and its bottom is often eroded. With the meningiomas of the lesser wing, as well as with other tumours of the temporal fossa, irregularities of the sella may be encountered. Probably the lesions are due to direct pressure by the tumour on the flank of the sella.

Calcification in the tumour itself.—With a relatively large number of meningiomas, in the tumour itself a calcification occurs. Formerly those tumours were called psammomas. If on a stereophotograph one sees such a calcified tumour on the sphenoidal ridge, partly in the middle cranial fossa, one may state quite readily that this is a meningioma.

Conclusions

In our case, we find by clinical examination the syndrome of Forster-Kennedy, exophthalmos and ophthalmoplegia. The syndrome of Forster-Kennedy is often encountered in lesions of the frontal lobe. It has been described by Kennedy in meningiomas of the olfactory triangle; with meningiomas of the lesser wing with an extension to the anterior cranial fossa it is no rare phenomenon.

The roentgenological data were:—erosion of the lesser wing on the affected side; local hyperostosis on the affected side; dilatation of the bony canal of the middle meningeal artery; and no changes of the sella.

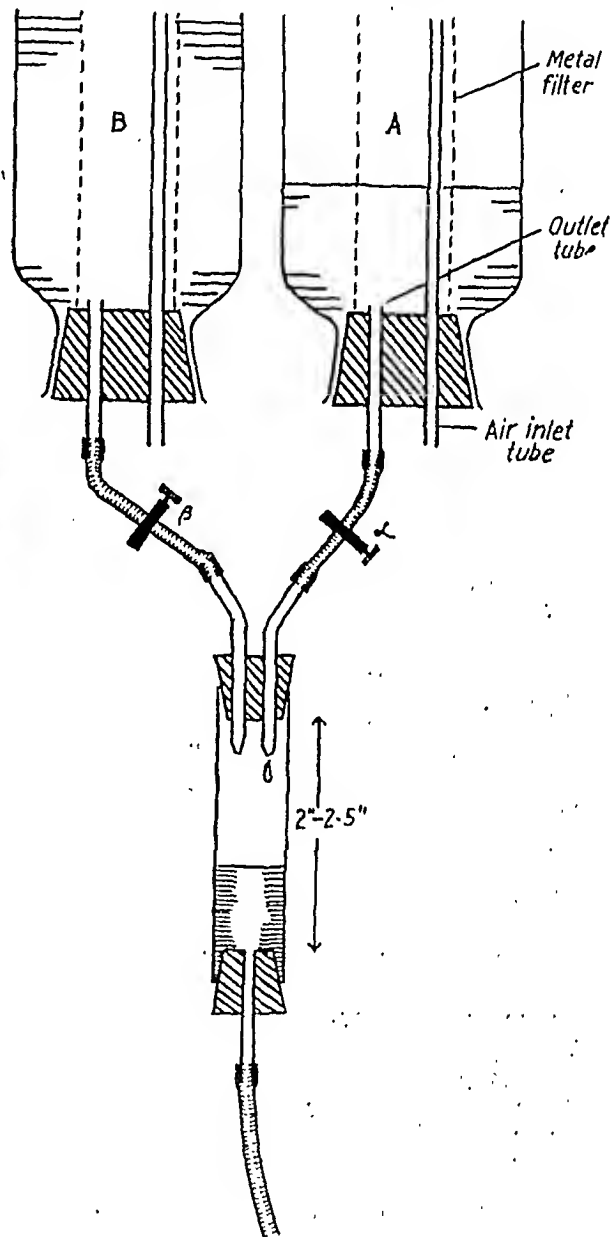
All these facts considered together point to a diagnosis of meningioma of the lesser wing of the sphenoid:

AN EFFICIENT AND EASILY CONSTRUCTED DRIP-REGULATOR FOR TRANSFUSIONS

By P. J. WORMALD, M.B., B.Ch. (Cantab.)
MAJOR, I.M.S.

No new ideas are to be seen in this apparatus, but it has been found to work admirably for regulating the speed of transfusions and infusions, given either rapidly or as a slow drip over a long period.

The diagram is self-explanatory. The use of two drip-nozzles is a great advantage in facilitating a quick change-over from one bottle to another. Thus (see diagram), when bottle 'A'



is empty screw-clamp 'a' is closed and screw-clamp 'b' is opened to the required amount. Bottle 'A' can then be changed at leisure. Another advantage in having two-drip nozzles is
(Concluded on opposite page)

CANCERUM ORIS AND ALLIED CONDITIONS

By M. N. DE, M.B. (Cal.), M.R.C.P. (Lond.), F.N.I.

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First Physician, Medical College Hospitals*

*(From the Department of Medicine, Medical College
Hospital, Calcutta)*

THE subject of gangrenous stomatitis does not appear to have received the attention it deserves from the general medical profession. Diverse ideas about its incidence and ætiology are still current in different parts of the world. The descriptions given in the various recognized test-books of medicine, written both in the old and

(Continued from previous page)

that if, for instance, isotonic glucose and isotonic saline are being administered, the desired amount of each can be given from separate bottles.

In commencing transfusion, while filling the drip-chamber and tubing with blood before inserting the intravenous needle or cannula, it is, of course, necessary to loosen the top cork while filling the chamber to the desired level, in order to allow the escape of a corresponding amount of air from the chamber. Once set up, the apparatus requires no attention except the regulation of the drops to the desired rate and the shaking of the bottle every quarter of an hour or so if whole blood is being administered.

Construction. (a) *Tools.*—A blow lamp and cork-borers are needed.

(b) *Materials required.*—(i) Glass tubing, internal diameter 7/10 to 8/10 inch. Glass tubing, internal diameter about 3/20 inch.

(ii) Two rubber corks.

(c) *Practical points.*—(i) The internal openings of the drip-nozzles should not be smaller than 1/20 inch in order to allow for a good stream in rapid transfusions. It is, of course, necessary to find by experiment the volume of blood delivered by each nozzle for a given rate of drip.

(ii) Neat holes can be bored in rubber corks with the greatest of ease by means of ordinary cork-borers if the cutting end of the latter is dipped in a strong solution of caustic soda just before use.

(iii) Wide-bore glass tubing can be cut accurately and rapidly with a three-cornered file if the file is kept moistened with turpentine.

(iv) Drip-nozzles are fashioned and the edges of glass components are rounded off in the blow lamp.

I have used this drip-regulator extensively during the last six months for all types of transfusions and infusions, and for efficiency, robustness, and the ease with which it can be constructed and kept clean, it is much to be preferred to many commercial drip-bulbs. Moreover, in these days, such an apparatus is hard to obtain.

new world, are of little help to a medical man practising in the tropics. In fact all the ætiological factors which are known in its connection in our country are hardly considered in the European and American continents, and this discrepancy may be attributed to lack of adequate exchange of views regarding the different clinical conditions in which cancerum oris occurs. A study of this subject, as well as of its allied conditions, may therefore be of interest to the medical profession.

In Europe and America, this morbid condition has been frequently described as characteristically a disease of children exhausted and devitalized by measles, scarlet fever, diphtheria or enteric fever. In adults, such a gangrenous process has been said to follow minor lesions in a foul mouth, specially in persons affected by syphilis or alcoholism, or suffering from mercurialism. But the classical picture of cancerum oris is rarely reproduced in the published descriptions of the conditions just mentioned.

As an epidemic, it had been reported in olden days in connection with scurvy in camps, jails, and ships, but these, again, were clinically different from true cancerum oris. None of the writers mentions the occurrence of the malady in certain tropical diseases, the most important of which are leishmaniasis, splenomegalic conditions, severe anæmias and other diseases which are characterized by extreme lowering of the body resistance. Measles has been described in Europe and America as being by far the most important disease in which cancerum oris occurs as a complication. Measles however is hardly found in India, where kala-azar and other forms of splenomegaly are the most common conditions associated with cancerum oris.

In our country, gangrenous stomatitis appears to have been so intimately associated with visceral leishmaniasis that it almost became a diagnostic complication; whenever one saw a case of cancerum oris one immediately pronounced the case to be one of kala-azar. This idea has, of course, had to be modified to some extent, in view of the present-day conception of the splenomegalic disease prevalent in Bengal. In a considerable proportion of cases in which this complication is met with, splenomegaly is of undetermined ætiology having no relationship with kala-azar. For want of a suitable name, these cases have been grouped, for the present, under the title of Bengal splenomegaly (Connor, 1933; Napier, 1935; De and Tribedi, 1939). Cancerum oris has also been found in some cases of severe anæmia and cirrhosis of the liver.

The pathogenesis of gangrenous stomatitis (cancerum oris) is very straightforward. The extreme lowering of the body's defences is the primary condition, and is commonly manifested by a marked depression of leucopoiesis, particularly of granulopoiesis, and by the blockage of the cells of the reticulo-endothelial system, or by a marked inhibition of their antibody-forming function. Both these factors are found to work

together in leishmaniasis, in which blocking of the reticulo-endothelial system leads not only to extreme leucopenia with granulo-cytopenia, but also, to a marked degree, to a diminished formation of immune bodies. The result is that any infective process in the body, however trifling it may be, rapidly progresses and may cause gangrene.

The mouth is a place which suffers constantly from minor trauma during eating and mastication of food. Under normal conditions of life, the wounds thus produced rapidly heal, and nothing happens. In a state of devitalization, however, no healing takes place. On the contrary, the injured mucosa becomes infected, and rapidly becomes gangrenous. The existence of pyorrhœa and ulcerative gingivitis are important predisposing factors to the development of such a complication.

Besides leishmaniasis, there is in our province a very common clinical syndrome which is accompanied by a great enlargement of the spleen and liver, and which may be complicated by cancrum oris in the later stages. These cases of splenomegaly form a definite clinical entity, and are characterized by their chronicity, by the presence of little or no fever during most phases of the disease, and by the development of varying degrees of anæmia. There is also a good deal of nutritional change in the body, and, in fact, such cases may bear a marked resemblance to kala-azar. The blood picture of these cases reveals a well-marked leucopenia, with diminution of the neutrophils, and increase of the mononuclear cells. All the factors which predispose to the development of cancrum oris in kala-azar, are also present in this group of cases. Thus it will be obvious that, from the presence of cancrum oris in a patient with splenomegaly, one cannot make the diagnosis of kala-azar.

The clinical picture of cancrum oris is very characteristic. It is curious that pain is usually not a prominent complaint of the patient. Starting from a breach of the mucous surface, especially on the inner aspect of the cheek, the disease spreads rapidly, both superficially and deeply, so that the cheek is quickly perforated. There is considerable œdema, and the patient is unable to open his mouth properly. Within a short time, usually 3 to 4 days, complete necrosis occurs, the area becoming bluish in colour and ultimately sloughing away. The breath becomes extremely offensive, and there is copious stinking discharge from the mouth. Nevertheless, the patient may retain his appetite, and be able to take a fair amount of food. In one case that the writer has seen, the food was pushed by the patient himself through the narrow slit of the unaffected side of the mouth. The condition may be fatal within a surprisingly short period, but some cases do ultimately recover. In a favourable case, a sharp line of demarcation develops, and the healing of the necrotic area takes place by granulation. When this happens, a large amount of scar tissue is

formed, producing various types of deformities and ankylosis in the cheek and jaw.

This kind of gangrenous complication may also occur in various sites other than the mouth area. The uterine cervix, which is often a seat of trauma and infection, may be involved. The writer has seen one instance of noma of the cervix uteri developing in a patient suffering from kala-azar. During life, the condition was diagnosed as carcinoma of the cervix, but in the autopsy room a sloughing necrotic cervix uteri was found. A complete case note with a photograph was published in this journal by the writer (De, 1923).

The large gut is another organ which may develop this morbid complication. During the course of autopsy examinations on cases dying of kala-azar and splenomegaly conditions, the writer has seen a few instances in which the whole cæcum had undergone a gangrenous process, with marked swelling and a dusky coloration. During life, these cases developed terminal colitis with very offensive stools and marked toxæmia. A clinical diagnosis of gangrenous dysentery was made by the physician. It is obvious that the chronic devitalizing factors brought about by leishmaniasis or splenomegaly led to this gangrenous process, which might have started from an infected ulcer in the cæcum. In our country, the primary infection may start from an amœbic ulcer which is so common in the cæcum. As the pathogenesis of this condition is similar to that of cancrum oris, it may be termed 'cancrum intestinalis', or 'noma of the cæcum'.

A similar gangrenous condition sometimes takes place in the lungs. It has been found that a weak and anæmic patient, exhausted by a chronic splenomegaly disease, ultimately develops pulmonary infection, and dies of a terminal broncho-pneumonia. In some of these cases, the pulmonary infection proceeds rapidly to gangrene of the lung, with a severe degree of toxæmia, a high temperature and stinking dirty sputum. At autopsy, the typical picture of gangrene of the lung may be seen. The pathogenesis of this condition is exactly the same as that of cancrum oris, viz, primary loss of resisting power, and the development of broncho-pneumonia, the latter terminating in necrosis and gangrene. Such a condition may thus be called 'cancrum pulmonalis' or 'noma of the lungs'.

Necrosis and gangrene of the skin and subcutaneous tissues of the external genitalia have also been known to occur. It has been found in small girls, involving the tissues of the labia majora and extending above to the mons veneris. The whole area is converted into a mass of necrosis, blackish-green in colour and very foul smelling. The surrounding areas are swollen and œdematous. In favourable cases, the entire necrotic mass sloughs, forming a line of demarcation, and then healing by granulation. In bad cases, the lesion extends rapidly and widely, and the patient dies of toxæmia, or secondary infection of the lungs. As the pathogenesis is similar

to that of cancerum oris, this condition has been termed 'cancerum vulvæ' or noma pudendi. Such cases are not common.

Necrosis and gangrene of the external genitalia in the male is still more uncommon. The writer had never seen it, nor has he known such a case to be reported in the literature. Recently one case came under his observation in the Medical College Hospital.

He was an adult male, 32 years of age, a street-beggar by occupation, living amongst a group of similar men. He was brought to the clearing-room by an ambulance, in a very weak and debilitated state. He was found to be extremely weak and emaciated, and to be running an irregular pyrexia. Both the liver and spleen were markedly enlarged. The whole of the skin of the scrotum had sloughed away a fortnight before, leaving a dirty-looking ulcerated surface covered with sloughs and infested by maggots (*see photograph*). Both the testes were exposed, but their size was normal. The regional lymph nodes were enlarged and tender. When the slough was separated, a well-defined line of demarcation could be seen.



The blood picture was as follows:—Hæmoglobin 60 per cent; total red cells 3,100,000 per c.mm.; total white cells 5,125 per c.mm.; polymorphonuclear neutrophils 54 per cent; lymphocytes 40 per cent; monocytes 4 per cent; and eosinophiles 2 per cent; no malaria parasites were detected. Both the aldehyde and Chopra's tests were strongly positive. A sternal puncture was done and *Leishmania donovani* was demonstrated in the marrow. Suitable treatment of the sloughing ulcer together with adequate doses of urea stibamine improved the condition of the patient very rapidly.

Treatment of these gangrenous conditions should be prompt and persistent. The most important point is prophylaxis. Scrupulous care of the mouth and of all ulcerated conditions of the mucous membrane or any other part of the body is essential. At the same time, vigorous treatment should be directed to the primary cause.

When gangrene has already started, rigorous antiseptic treatment together with attention to the primary disease should be undertaken. Attempts should be made to maintain adequate nutrition of the patient. Massive doses of iron and vitamin C are beneficial. If the parts are accessible, the application of infra-red rays is very helpful in relieving tension and checking the further extension of the necrotic process. The scope of chemotherapy is very limited, owing to poor leucocytic reaction, but it should be tried. Tablets of any form of sulphanilamide if the patient can swallow, or injections of soluble preparations of the drug, may be helpful. Of the local applications, painting the part with trichloroacetic acid is sometimes beneficial. If anaemia is marked, transfusion of blood may be tried.

Acknowledgments

I take this opportunity to express my gratefulness to Dr. B. P. Tribedi, Professor of Pathology, for the photograph, and to Lieut.-Colonel H. E. Murray, I.M.S., Superintendent, Medical College Hospitals, for his permission to publish the records of the case.

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A Mirror of Hospital Practice

A CASE OF DATURA POISONING FROM EXTERNAL APPLICATION

By PHANI BHUSAN MUKERJEE, L.M.P.

I WAS asked to see a male child, aged 2 years. **Complaints.**—The relatives said that the child was delirious and restless, and could not recognize anyone. **Present illness.**—Eighteen days ago, the boy was attacked with fever attended with shivering. The fever lasted for 24 hours and then subsided. He kept well for 3 days; the fever relapsed on the fourth day, lasted again for 24 hours, and then came down, but during this attack, the child developed delirium, talked incoherently, and became restless. The guardians consulted a *vaidya*, who prepared an oil with *datura* seeds for external application in order to cure the disease or quieten the child. The oil was applied from the seventh day onwards. Three days after, the child became more restless, lost all sleep, and developed twitchings of his limbs. He had been in this state for 8 days, when I saw him.

Present condition.—The child was found screaming frequently with fright, tossing to and fro in his bed, lying in the dorsal position and unable to sit up. Sometimes, he was staring at a person with a vacant look but could not discern him. He did not respond even to a loud call. He was making ludicrous movements of his hands, talking at times indistinctly. He was thirsty owing probably to dryness of the mouth and throat.

There was no rise of temperature; pulse—regular, good tension, but a little quick; pupils—dilated; tongue—dry; abdomen—normal; the liver and spleen were not enlarged; bowels moved once a day; urine passed freely. There was no abnormality of the lungs and heart. Reflexes—normal.

Diagnosis.—I diagnosed the case to be one of *datura* poisoning, probably due to absorption of the poison in the oil which was being besmeared over his body continually for several days, the skin of an infant being delicate.

Treatment.—I prescribed a mixture containing liquor morphine hydrochloride mins. ii per dose. After 4 days, the child became quiet and began to sleep, but the movements of his limbs persisted. Therefore, on the 27th day, I added potassium bromide grains ii and one minim more of the liquor morphine hydrochloride to each dose, and the child was cured.

OVARIAN CYST IN A NULLIPAROUS WOMAN

By I. S. MARWAH, M.B., B.S. (Hons. Punjab),
L.M. (Rotunda), D.G.O. (Dub.), F.R.F.S. (Glas.)

Chief Medical Officer, Sirmur State, Punjab

OVARIAN cysts of the pseudo-mucinous type are well known for their rapid development and the large size they attain. Recently, I removed one weighing 55 pounds. The notes of the case are given below :—

Patient, aged 20 years, was admitted to the State Zenana Hospital, with an enlarged and distended abdomen. The history of the illness was that she was married at the age of 15 years. Menstruation started at 16, when she complained of an enlargement in the abdomen starting from the right iliac fossa, with irregular menses, twice or thrice a month. In a couple of years the enlargement attained the size of a full-term pregnancy. At this time the menstruation completely stopped. After that the enlargement went on at a more rapid rate till it filled up the whole of the abdomen.

On physical examination the abdomen was found tense, with enlarged veins running up to the epigastrium; the lower ribs were markedly pushed out. A fluid thrill was present in the abdomen and could be felt in the fornices on P.V. examination. No shifting dullness was present. The heart and kidneys were normal. On P.V. examination a small uterus pushed to the opposite side could be felt. The patient's weight was 130 pounds. The abdominal girth at the most prominent point was 37 inches. A diagnosis of right ovarian cyst was made.

Operation.—After a preliminary morphine and atropine injection, and under chloroform anaesthesia, the abdomen was opened in the middle line from pubis to the umbilicus. Difficulty was experienced while opening the peritoneal cavity, the tumour being closely adherent to the parietal peritoneum. With considerable difficulty and caution, a little of the parietal peritoneum was peeled off the tumour. The cyst was then tapped with a trocar and cannula, and about two-thirds of its contents, dark brownish fluid, not unlike the anchovy sauce of the liver-abscess pus, were removed, and the opening was closed with a purse-string suture. The whole of the peritoneum was found firmly sticking to the tumour, and had to be separated with gloved fingers and at places by a blunt director. Its top was adherent to the under surface of the diaphragm, and great difficulty was experienced in peeling it off. The pedicle which was about 6 inches long was ligatured, and the tumour was removed. The other ovary was inspected and found slightly enlarged and cystic. The abdomen was closed in the usual manner. The tumour and its contents weighed 55 pounds thus leaving a balance of

75 pounds only as the weight of the patient. She stood the operation very well and had an uneventful recovery.

The interesting features of the case are as follows :—

1. The size of the tumour. Such large tumours rarely come to the notice of the profession.

2. The age of the patient. Ovarian cysts are usually met with in middle-aged women. My presumption in this case is that proliferative activity in the ovary started with the onset of puberty and resulted in the formation of the tumour. In the early stages it gave rise to excessive and increased menstruation, but when the degeneration started in the ovarian tissue, the menstruation completely stopped.

3. The difficulty that was experienced in removing the tumour, and particularly the fact that it was sticking to the parietal peritoneum without a single adhesion which needed a ligature.

4. The uneventful recovery of the patient after the removal of more than one-third of her body-weight.

I am grateful to my assistants Dr. U. C. Mukerjee and Dr. (Miss) K. K. Bhatnager, who assisted me at the operation and carried out the post-operative care of the patient.

RETENTION OF THE PLACENTA

By RAO SAHAB T. D. RAJOO

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THIS is a review of cases treated here for retention of the placenta during the last 9 years. During this period 18,591 women were confined, of whom 64 had retained placenta due to uterine inertia, contraction ring, or adhesions of the placenta or membranes. Fifty patients were cured, 4 were discharged otherwise and 10 died, giving a mortality of 15.62 per cent (see table I).

The third stage of labour is left to nature. At the end of half an hour, if the placenta has not been expelled naturally, an effort is made to express it by Credé's method. If it cannot be expressed and if there is no bleeding, further interference with the uterus is stopped and 400 c.cm. of sterile normal saline solution is injected into the umbilical vein. Out of 37 cases so treated, in 16 the placenta was expelled spontaneously, or by Credé's method (see table II).

When manual removal becomes necessary, the patient is given a general anaesthetic, usually chloroform, and with strict surgical aseptic technique the hand is introduced into the uterus and, if possible with one sweep, the placenta with membranes is removed, the re-introduction of the hand being thus avoided. If there is spasm due to contraction ring, the patient is given amyl nitrite inhalations while the hand is being introduced. After the removal of the placenta, a hot intra-uterine douche is given, and pituitrin or

ergometrine is injected hypodermically. The patient is treated for shock should it be necessary.

In spite of the aseptic precautions taken, 32 cases ran a temperature for a few days, and 2 cases died of sepsis.

I am grateful to Colonel J. C. Pyper, O.B.E., I.M.S., for encouraging me to write this note and to Dr. S. H. Ramgopal, for assisting me in compiling the statistics.

TABLE I

Number of confinements in 9 years	18,591
Number of retained placenta	64
Rate	0.34 per cent
Number cured	50
Number died	10
Number otherwise discharged	4
Death rate	15.62 per cent
Number of cases that ran a temperature.	32
Number of cases that had saline in the umbilical vein.	37

TABLE II

Adherent placenta	40
Simple retention	24
Placenta removed manually	45
Expelled after saline injection and by Credé's method.	14
Expelled spontaneously	2
Placenta not removed	3

TABLE III

Causes of death—	
Heart failure	4
Post-partum hæmorrhage	4
Sepsis	2

EXTRA-UTERINE PREGNANCY WITH A FULL-TERM LIVE FŒTUS

By S. R. GORUR, M.B., B.S. (Bom.)

District Medical Officer, Sri Narasimharaja Hospital, Kolar

THE following case is reported on account of its rarity. Abdominal pregnancies are reported, but those going on to full term are very rare.

A Hindu female, aged 32, was admitted for full-term pregnancy with labour pains. She was a small-built woman, anæmic and weak.

Previous history.—This was her eighth pregnancy. Previous labours were all normal. The course of this pregnancy too was normal, with no pain, colic, prostration, etc.

Present history.—The patient had reached full-term, and labour pains started, so she sought admission to the District Hospital. Pulse 86, respiration 26, temperature normal. The blood picture was that of anæmia of pregnancy. Urine examination—no abnormality detected.

On inspection the abdomen appeared unduly and unevenly prominent; the left flank appeared more full. There were contractions (mock labour) coming off and on, accompanied by pain. On palpation, the fetal

parts were very conspicuous. The fetal head was prominent on the left side low down, and the limbs were palpated higher up across the middle line. Auscultation revealed clear fetal heart sounds but not the usual souffle.

On bimanual examination, the contour of the uterus could not be definitely made out. The cervix was high up and did not correspond in size and consistency with that of a normal full-term pregnancy. The os was slightly dilated and soft. There was no presenting part, and no ballotment could be elicited. There was neither discharge nor 'show'. The patient was kept under observation for two days, and was in great agony; hence exploration was undertaken. The abdomen was opened under chloroform anaesthesia. The uterus was found to be of the size of a coconut. The fetus was in its sac, lying in the peritoneal cavity amidst coils of intestines confined to the left side. There was a loop of cord round the left ankle of the fetus. This was released, and, the cord having been severed between clamps, the fetus was delivered. Soon after it was handed over to the nurse in attendance, it started to cry. The child was healthy. The placenta, measuring about 7½ inches by 5 inches, was attached to the broad ligament, mostly on the left side, and spread over to the right, behind the uterus.

Soon after the fetus was delivered, bleeding from the placenta started. The field of operation could not be seen, due to the welling up of blood. As the last resort, the uterine vessels were clamped over the broad ligament, and hysterectomy was done. While the bleeding was being controlled, intravenous saline-glucose was administered. The abdomen was closed and the patient was returned to the ward, but in spite of all subsequent treatment, the patient died six hours later.

The child was healthy, well built and normal but for the slight talipes deformity of the left foot. It was taken home and is reported to be living.

X-rays and photography were not available.

Outstanding features were the complete absence of history and signs of extra-uterine pregnancy until full term and admission to the hospital; and the delivery of a full-term viable healthy child.

My thanks are due to Dr. V. V. Monteiro, Senior Surgeon in Mysore, Bangalore, for his suggestions and to Dr. Kokila Ramabrahma for her aid in the clinical examination and during the operation.

SERUM SHOCK AND SERUM REACTION

By K. G. IYENGAR

Assistant Surgeon, King Edward Memorial Hospital, Secunderabad

SERUM reaction manifesting itself in the form of urticaria about a week after the injection, is fairly common, but shock is rather a rare occurrence. During the twenty-two years of my service and practice, I had not met with a single case of serum shock. Recently I was myself a victim, and I therefore give a description of my experience.

On the 3rd July, 1942, at 8-15 a.m. I was given a prophylactic dose of anti-tetanic serum (1,500 units in 1 c.cm.) intramuscularly, for a small

injury on my heel. I continued my routine work for about half an hour, and then suddenly felt a peculiar sensation of heat all over the body. In a few minutes, I felt a tightening in the chest, and had to struggle for breath; I developed cyanosis. One of my colleagues gave me an adrenaline injection $\frac{1}{2}$ c.cm., which eased my respiration. Shortly afterwards my body became studded with an urticarial rash, and I started to vomit. The whole day I tossed restlessly in my bed with a strange feeling in the chest and abdomen. I had a splitting headache and could not sleep in spite of hypnotics. The cyanosis gradually decreased and disappeared after 36 hours, and for the next two days I was comfortable.

On the 4th day of the illness I had frequent attacks of colicky pains in the abdomen, which persisted for two days. These symptoms subsided without any special treatment.

On the 6th day urticaria reappeared, and that rather suddenly, and persisted for 36 hours in spite of adrenaline and calcium gluconate injections. I felt weak for nearly fifteen days after this experience.

In the recent *Textbook of Medical Treatment* by Davidson, Dunlop and McNee (page 75) it is stated that intravenous, intrathecal and intraperitoneal injections of serum are more apt to produce severe and rapid anaphylactic symptoms than intramuscular or subcutaneous injections. For over ten years I have been treating all cases of tetanus in this hospital by intrathecal (20,000 units in 10 c.cm.) and intravenous (80,000 units in 40 c.cm.) injections. So far I have never observed in my patients any trouble of this serious nature; but urticaria has been a fairly common phenomenon.

After my recovery, an experienced doctor-friend of mine casually remarked that I had made a lot of fuss over a little 'serum reaction'. If the patient is a lay person, many doctors are prone to interpret restlessness in such cases as 'fuss' and label the poor man 'psychoneurotic'. To adopt such an attitude without making a thorough and prolonged examination is neither fair to the patient nor to the profession. In the book quoted above (page 849) it is stated that serum reaction, if not properly and effectively treated, may result in the death of the patient. At the moment of taking the injection I gave no thought to the possibility of my being an anaphylactic individual. Since 1926 I have had, very occasionally, light attacks of asthma, and urticaria thrice. I suffered from catarrhal jaundice thrice in my life, and frequent attacks of 'cold' during the last three years.

I do not discuss treatment, as this note is meant to give merely a description of my experiences.

My thanks are due to Lieut.-Colonel J. C. Pyper, O.B.E., I.M.S., our medical officer, for kindly permitting me to publish the above facts.

VAGINITIS DUE TO *ENTAMOEBA HISTOLYTICA*

By MA YIN MAY, M.B. (Cal.), M.R.C.P. (Edin.),
F.R.C.S. (Edin.)

Late Honorary Gynaecologist, Ramkrishna Mission
Hospital, Rangoon

Ectopic lesions due to *Entamoeba histolytica* have been described, but I have been unable to find a record of a case similar to the one about to be described. Its rarity and the complete relief of symptoms by specific treatment with emetine have encouraged me to publish it.

Case record

An Armenian girl, aged 24, was brought to me in 1938 by her mother for the following complaints:—

Leucorrhœa for about three weeks, and excoriation of the vulva and neighbouring areas. Menstruation was regular and symptomless. There were no other symptoms.

Both the mother and the patient were much upset by the condition, as the girl was to be married within a few months.

Previous history.—The patient had always maintained good health. She gave no history of dysentery.

Physical examination.—The patient was a well-built girl. General examination was negative. The patient was unusually shy and would not allow a thorough gynaecological examination. There were definite signs of vulvitis and vaginitis, though the inflammatory reaction of the latter was quite mild. The hymen was intact but admitted a finger loosely. Rectal examination of pelvic organs indicated a normal sized uterus, and no abnormality in size or tenderness of adnexa.

Laboratory diagnosis.—Smears were taken by means of a sterile platinum loop from the urethra and vagina. The laboratory report from the Pasteur Institute indicated a doubtful gonococcal infection. The patient was questioned and persisted in her assertion of her virginity, so I approached Lieut.-Colonel G. C. Maitra, I.M.S., the Director of the Pasteur Institute at the time, to help me in the diagnosis. Fresh specimens were taken and coverslip preparations showed active *Entamoeba histolytica*.

Treatment.—The patient recovered completely under a course of emetine injections with very little local treatment.

Discussion

The commonest clinical diagnosis of such a case would be gonococcal infection. Very rarely would other causative organisms be implicated. The presence of active *Entamoeba histolytica* surprised both Colonel Maitra and me. The response to treatment was also satisfying. If laboratory facilities had not been available, the diagnosis would have been in doubt, and the patient made to undergo fruitless treatment and also to suffer an unmerited stigma of a suspected venereal infection. It is thus important to remember *Entamoeba histolytica* as a possible cause of vaginitis.

The mode of infection could only be surmised. The patient was accustomed to taking her bath in the western manner—sitting in a bath-tub—and infection may have occurred from this source.

I have to thank Lieut.-Colonel G. C. Maitra, I.M.S., for taking so much trouble in personally undertaking the laboratory examinations.

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REGIONAL ILEITIS (CROHN'S DISEASE)

SINCE in 1932 Crohn and his associates drew attention to this relatively uncommon disease, numerous papers have appeared on the subject in America and later in England. The condition is now being recognized in this country. In a paper that appears in this issue, Dr. S. D. Arawattigi gives a résumé of the subject, with brief notes of five cases out of twenty-six encountered during a period of four years. Our contributor has referred to a number of foreign publications, but seems to have overlooked at least two Indian ones, viz, the papers by Dr. Manohar and Dr. Kini published in this journal in May and November 1941.

A perusal of the literature shows that the condition was recognized long ago. For instance, in 1806 Coombe and Saunders described 'a singular case of stricture and thickening of the ileum' which might well have been a case of regional ileitis. Since then, a number of similar isolated case reports have been published. Perhaps the most important contributions were made by Moynihan in 1907 and Braun in 1909, the condition being discussed under inflammatory tumours of the intestinal tract.

The disease under consideration is an inflammatory granuloma of the intestine. The aetiology is still quite obscure. In the past the condition has generally been confused with ileo-cæcal tuberculosis, because of certain pathological findings, namely, granulomatous change with giant cell formation, etc., but tubercle bacilli are never found in the lesions, and guinea-pigs inoculated with the tissues never develop tuberculosis. Some workers attribute it to bacillary dysentery infection, but others have been unable to confirm this. Our contributor suggests that the formation of adhesions after appendicectomy, and *Entamoeba histolytica* infection are possible predisposing factors; this requires confirmation. There are points which indicate that amœbic infection may play little or no part in the causation of this condition; for instance, the ileum is hardly ever involved in amœbic dysentery and the hypertrophic stenotic lesions are unusual. Many observers have failed to find *E. histolytica* in the stools of cases of regional ileitis, and this condition did not respond to specific therapy. It appears therefore that *E. histolytica* is probably a secondary invader, or an associated infection in this disease.

It is possible that a variety of factors may initiate the inflammatory process, which is augmented by an infection or irritation of the intestinal content. In this connection, the experimental studies of Reichert and Mathes are worth

mention. They injected irritating and sclerosing solutions into the mesentery and produced an 'elephantoid' condition of the bowel simulating the earlier stages of regional enteritis. This suggests the possibility that the primary lesion of Crohn's disease may be an obstructive lymphangitis in the mesentery, as mesenteric changes are invariably associated with regional enteritis. In the early stages, the affected portion of the mesentery is congested and the lymph nodes are enlarged. In the later stages, the mesentery is considerably thickened, and shows fibrotic changes similar to those seen in the diseased bowel.

The disease usually involves the terminal part of the ileum, so that the designation 'terminal ileitis' was originally used by Crohn, but other segments may be affected; consequently, numerous names have been suggested and applied to this disease. These terms are, however, mostly descriptive of the region of the affected bowel, and give no information as to the nature of the lesion. Probably, the most accurate term would be 'non-specific inflammatory granuloma' specifying the region of the intestine involved. The diseased portion of the bowel becomes thick, œdematous and red. Active inflammation is followed by fibrosis, and the lumen is progressively narrowed. The bowel may become adherent to surrounding structures, and the inflammatory process may lead to the formation of abscesses and sinuses. Sometimes, the case is wrongly diagnosed as one of chronic appendicitis, is operated upon, and the appendix is removed without the real nature of the disease being realized. Fistula formation is very apt to follow such operations.

Four phases of the disease have been described as following one on the other, but this course is variable. The early phase resembles an attack of appendicitis, acute or sub-acute, with colicky pain, fever, tenderness and perhaps a mass in the right iliac fossa and bowel irregularity. Later, the symptoms resemble those of ulcerative colitis, with passage of blood and mucus. Later still, with the narrowing of the lumen of the gut, symptoms of obstruction may appear, and, with loss of weight, may be attributed to malignant disease or tuberculosis. Finally, there is the stage of sinus and fistula formation which may be attributed to tuberculosis or actinomycosis.

A thorough and careful roentgenological examination is of great value in diagnosis. The portion of the bowel proximal to the stricture is dilated and may contain fluid and gas. Filling defects are seen in the affected portion. This is called the 'string sign of Kantar' and indicates stenosis. A thin, tape-like, irregular shadow like a cotton string (hence the name) often passes from the distended coils of the ileum through the filling defect to the cæcum. While it is very suggestive, this 'string sign' is not pathognomonic, and its absence does not exclude regional ileitis.

In treatment, chemotherapy has been tried with poor results. X-ray therapy has proved futile. Once a diagnosis of the condition has been made, surgery is the method of choice in treatment, especially when signs of beginning obstruction are present. The exact procedure depends on the stage of the disease and the condition of the patient; it may have to be decided by exploratory laparotomy.

If we bear in mind the possibility of the occurrence of this disease in all patients with an obscure mass in the lower abdomen; then with the aid of skilled radiography and with co-operation between physicians and surgeons, the recognition and early diagnosis of more cases in this country will be facilitated.

R. N. C.

DR. L. EVERARD NAPIER

DR. NAPIER, for many years editor of this journal, has left India.

We do not wish this note to be mistaken for an obituary notice, or even for a note written on a man's retirement from active work, for Dr. Napier is very much alive, and he is not even retiring, but is assuming a responsible position in another country. We feel, however, that some notice of his work should appear in the journal which he served so long and well.

He qualified in medicine in 1914, served in the R.A.M.C. from 1915, in the Mediterranean and in Egypt, in hospital ships and transports. Later, he served in Mesopotamia, as it was then called, where he succeeded Acton as pathologist, and also in Bombay, where he succeeded Knowles as pathologist. Thus in war were forged his early links with tropical medicine.

Later, both Acton and Knowles were designated as professors of the new School of Tropical Medicine, Calcutta, and Knowles persuaded Napier to return to India from England, which he did in 1920 and shortly joined the School as research worker in kala-azar. Kala-azar was his main sphere of work for fifteen years, and his reputation became world wide, for he made important contributions to knowledge of epidemiology, aetiology, transmission, diagnosis, treatment and in fact to every branch of the subject. He was early convinced that the sand-fly was the vector, and strove to prove this experimentally. He never succeeded, for knowledge of the bionomics of the sand-fly was inadequate. It was, however, a fitting crown to his work that shortly before he left India, the scientific proof was completed by men who had been his co-workers.

In 1935 he became Professor of Tropical Medicine in the School of Tropical Medicine, Calcutta, a position which he filled with distinction. Later, he became the Director of the School.

His contributions to knowledge of tropical medicine were numerous and valuable. In addition to his work in kala-azar, he made important

contributions to knowledge of malaria, anaemia and other subjects. His work on anaemia in India has been outstanding. His knowledge was very extensive and thorough, and his help and advice was much sought by workers (including the present writer who owes much to him) on many of the problems of tropical medicine.

As a writer, he was well known for his book on kala-azar, for his contributions on the subject in standard works of reference, and for his many articles in the medical press; but also for his work on the *Indian Medical Gazette* of which he was assistant editor for five years, and editor for ten. In this journal he maintained a high standard. His more scientific articles were along more conventional lines, but an editorial or a review written by Napier was easily spotted by those who knew him, for he had his own style and mannerisms which were excellent in his hands, but which it would be inadvisable for others to attempt to imitate (the present writer knows how Napier will chuckle when he reads this last sentence!).

Others however might well try to attain his breadth of vision, and to adopt his readiness to attack and to discard generally accepted views if there was real evidence against them. He critically examined all accepted views, and only adopted them and taught them if he thought that they were based on sound evidence.

Napier, in recognition of his published work, attained the very rare distinction of being made a member of the Royal College of Physicians, London, without examination. He was later elected a fellow. He was last year awarded the C.I.E. His greatest distinction is that he has left a very definite mark on the practice of medicine in India. As he himself always acknowledged, his work was made possible by the assistance of a number of able Indian research workers, who fortunately are still carrying on and developing several important lines of work.

The memory of Napier in India should be kept green by his 'Principles and Practice of Medicine in the Tropics', the first part of which is now in the press. It is being published in India. It should become a standard work not only in India but in other countries.

J. L.

Special Article

THE DANGER OF EXPLOSION OF ETHER-AIR MIXTURES IN THE OPERATION THEATRE

By RAI BAHADUR K. N. BAGCHI, B.Sc., M.B., D.T.M.,
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Chemical Examiner to the Government of Bengal,
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IN places where there is no electric supply, 'open lamps', such as petromax, ordinary kerosene lamps or acetylene gas burners, have been commonly used for performing surgical operations

after sunset. In the event of a breakdown of the electric supply system, surgical operations may have to be performed even in cities such as Calcutta, in the presence of open lamps. During an air raid, especially if it is a prolonged one as happened on the 24th December last in Calcutta, the closing of door and window shutters and ventilators to enforce complete black-out stands in the way of maintaining proper ventilation in operation theatres, and therefore the possibility of accidents from the explosion of ether vapour during ether anaesthesia has to be seriously considered. In fact the question has already been engaging the attention of the authorities. A knowledge of the important features of ether and the ether-air mixture used for anaesthesia should help us in devising precautionary measures against accidents likely to occur in operation theatres, and also in handling ether properly, especially in the presence of a naked flame.

The best available discussion of this subject is that of von Schwartz, which was written as long ago as 1904. Much of the information given here is quoted from his book.

General properties

Ether, sulphuric ether or ethyl ether, as it is called, is a highly volatile and inflammable liquid, the vapours of which form explosive mixtures with air or oxygen when mixed in certain definite proportions. Its boiling point is 95°F. (35°C.) which is lower than the body temperature and is about the same or even lower than the room temperature during the hot months in Calcutta. Warmed ether tends to boil over, and if the vapour comes into contact with the open flame of the burner, it may catch fire. It does not mix with water, and if a mixture of ether and water is shaken and then put aside for a few seconds, the two layers separate, and ether, being lighter than water, forms the top layer. This treatment with water does not mitigate the inflammability of ether. The vapours of ether are about 2½ times heavier than air, and therefore the vapours sink to the floor, where they tend to diffuse very slowly in all directions.

The action of air and sunlight on ether

Prolonged exposure to air and direct sunlight, as for instance by keeping half-filled bottles in a cupboard exposed to sunlight, brings about a partial decomposition of ether, with the formation of an unstable compound, vinyl alcohol, and hydrogen peroxide, both of which impart to the sample the property of exploding by heat (90°C.), percussion or violent shock (von Schwartz, 1904). Similarly, oxygen, ozone and certain substances known as carriers of ozone, such as oil of turpentine, oxidize ether, with the formation of a poisonous and highly explosive substance, ethyl peroxide, which may explode simply on heating but more readily by heating in the presence of fats or oils or other organic substances. For these reasons, ether should always be stored in a dark cupboard and in amber-coloured bottles filled up to the neck, to prevent contact with air

and sunlight. In the presence of oxygen, it is readily decomposed by red hot platinum wire into formaldehyde, acetaldehyde (Beilstein, 1918), etc., one molecule of ether yielding four molecules of formaldehyde.

Ether fires

If ether catches fire, it must be extinguished by cutting off the supply of air by closing the doors, windows and ventilators; otherwise an admixture of its vapour with fresh air in suitable proportions may cause a dangerous explosion. Water should, as far as possible, be avoided in extinguishing burning ether, since in running away, it may carry the burning ether to other parts of the room. The useful materials for extinguishing ether fires are sand, earth or ashes. CO₂ gas is, however, the best extinguisher of such fires.

If ether takes fire in the vessel in which it has been stored, it must be covered up immediately, because the burning ether is so rapidly vapourized by its heat of combustion that explosions are likely to follow; such explosions would scatter the burning ether all over the room, producing a serious conflagration. The CO₂ gas produced during combustion in the vessel thus covered, helps automatically in extinguishing the fire.

Ventilation of room where ether is used

As ether vapour is heavier than air, it sinks to the floor, and therefore the fitting of ventilating appliances such as exhaust fans, near the ceiling or in the roof, is fundamentally wrong. They are, no doubt, good for gases and vapours lighter than air, such as coal gas, acetylene, petrol vapour, hydrocyanic acid, carbon monoxide, etc., but in the case of ether, floor ventilation is necessary. If, however, the ventilator is a powerful one and the room is small and low, roof ventilation may be useful, but the draught thus produced in an operation theatre will not be desirable for surgical operations. For heavy vapours and gases, suitable small ventilators at the floor level will be far more efficient than powerful exhaust fans in the roof. In places where there is no electricity, or when the electric supply system has been dislocated by enemy action, the ventilation may be effected by swinging at the floor level, large hand fans (made of palm leaves as used in Indian homes in the countryside on ceremonial occasions) or similar contrivances.

The migration of ether vapour

As the heavy vapour of ether sinks by its own weight to the floor, any crack or fissure in the floor offers it an easy passage to the room below. It may also come out through open doors and, directed by the air current, may make its way down the stairs to a room below and be ignited there by an open fire such as a lighted stove, a lamp or a burning match. Here there may be an explosion or a simple ignition and flash according to the concentration of ether. If there is simple ignition, the flame will immediately

'flash black' along the current of the vapour to its source in the upper floor, and produce an explosion there—this is what is called 'explosion by remote fire' (von Schwartz, *loc. cit.*). This phenomenon accounts for fires or explosions in places where there is ether but no fire to ignite it. Experiments have shown that such accidents may take place within a range of 30 feet from the source of the ether vapour (von Schwartz, *loc. cit.*).

The ignition point of ether vapour

The lowest ignition point of ether vapour in air varies, according to different observers, from 190°C. to 360°C. (Dixon, 1926). This shows that there is a special danger in bringing a heated body in contact with ether-air mixtures. The temperature at incipient red heat, according to the German Physico-Technical Institute, is 525°C. The first emission of light occurs, in the case of platinum, at 390°C. and at higher temperatures in the case of other metals (von Schwartz, *loc. cit.*).

Notwithstanding the fact that authors differ in their estimations of the amount of heat necessary to produce red heat, the ignition point of ether is undoubtedly lower than the minimum figure quoted above. This observation indicates that the danger of ignition of ether vapour in the throat and mouth of the patient during cauterization by electro-cautery under ether anaesthesia is not negligible. In similar circumstances the decomposition of ether and production of formaldehyde (von Schwartz, *loc. cit.*) may also take place in the throat. As formaldehyde is a powerful irritant gas, its inhalation with ether is likely to produce harmful effects on the respiratory tract.

Electric sparks and the ignition of ether vapour

The production of even the faintest electric sparks in an atmosphere where there is an explosive mixture of ether vapour and air may produce explosions. Ordinary electric lights are considered as 'open lamps' and are placed in the same category as petromax or other kerosene lamps. In these lights, the bulb fits loosely in the socket (Peace, 1939) and a slight movement (as in pendant lights) produces, at the points of contact inside the socket, small sparks which may ignite the inflammable vapour penetrating into the fittings. The electric lights which are used in atmospheres containing inflammable vapours are, therefore, of a type manufactured specially for this purpose and are absolutely proof against such accidents. The use of cheap electric torches in such atmospheres may also be a source of danger.

The examination of the throat with an ordinary torch during ether anaesthesia is, therefore, to be discouraged.

Factors modifying explosibility of inflammable vapours

The limits of explosibility of various explosive mixtures of inflammable gases and vapours with

air are greatly modified by several factors which tend either to accelerate or inhibit the chemical actions bringing about the explosion. The presence of floating dust, especially of organic nature, increases the explosibility; for example, a mixture of marsh gas and air becomes explosive when the concentration of the gas is 5 per cent, but if any dust, such as coal dust (as happens in coal mines), lampblack, wood-dust, flour, etc., is present in the mixture, it is rendered more explosive, and the explosion takes place when the concentration is as low as 3 per cent (von Schwartz, *loc. cit.*). The action of ether under similar circumstances has not yet been worked out, but it is believed that ether too behaves in the same way. On the other hand, there are certain other substances which inhibit the reaction—CO₂ gas and moisture being important members of this group. The effect of the inhibitory action of CO₂ is remarkable, and that is why it is so well known as a fire extinguisher.

The concentration of CO₂ in air and its effects on ether-air mixtures and human system

The atmospheric air contains 0.04 per cent of CO₂ while the expired air of man contains about 4 per cent—the yield being 0.6 to 1 cubic foot of CO₂ per hour per head. The amount of CO₂ obtained by burning one pound of kerosene is about 27 cubic feet, which may be produced by a powerful petromax lamp in about two hours. In rooms with all doors and windows closed, the production and accumulation of CO₂ from both the sources may therefore be considerable.

The effect of CO₂ on the human system is interesting. The usual signs and symptoms of CO₂ poisoning as observed in overcrowded and ill-ventilated places are not really due to CO₂ but to other volatile substances or exhalations from the body, and also humidity. It has been observed that a concentration of as little as 0.5 per cent of CO₂ of respiratory origin produces toxic effects such as languor, headache, etc. If it reaches 6 to 7 per cent, dangerous symptoms of poisoning develop. On the other hand, in places where the origin of the CO₂ gas is other than the expired air of human beings, as for example, burning gas or kerosene lamps, brick or lime kilns, fermentation of sugar for alcohol, etc., a much higher percentage of CO₂ is required to produce toxic symptoms. Sydney Smith (1940) states that in an atmosphere containing 20 per cent of pure CO₂ one can breathe freely without noticeable effects (Smith, *loc. cit.*). In cases of fatal poisoning by CO₂, as may occur in persons at the bottom of old wells or fermentation vats or in persons sleeping near lime kilns, death is due to a much higher concentration of the gas, as high as 60 to 80 per cent.

The amount of CO₂ necessary to extinguish fire varies widely, and depends on the kind of flame, i.e., on the chemical composition of the burning substance. For example, marsh gas requires only 10 per cent, while kerosene flame requires 15 per cent and coal gas 33 per cent.

of CO_2 (von Schwartz, *loc. cit.*). We have found by actual experiments that a concentration of about 20 per cent by volume of CO_2 prevents completely the ignition of an ether-air mixture containing 6 per cent of ether vapour. Proportions less than 20 per cent of CO_2 modify the inflammability but do not stop it. Operation theatres may, therefore, be rendered immune to ether fires if the concentration of CO_2 in the air is raised to 20 per cent, but it is hardly possible to increase the concentration of pure CO_2 without the admixture of an appreciable amount of CO_2 of respiratory origin even when the ventilation is completely shut off. There is, however, no doubt that a considerable amount of CO_2 is produced which, along with the moisture produced simultaneously, goes a long way in reducing the explosibility as well as the inflammability of ether-air mixtures likely to be formed there, especially when all communications with external air have been completely cut off.

The concentration of ether in air required to produce anæsthesia

It has been stated by Sollmann that light operative anæsthesia requires 5.6 per cent by volume of ether vapour in air (or 18.5 mg. of ether per 100 c.cm. of air), while deep anæsthesia requires 10.5 per cent (or 34.6 mg. per 100 c.cm. of air). If this limit is exceeded even by half per cent, it proves fatal. The concentration of ether vapour under the mask usually averages, after 10 minutes of anæsthesia, 7 per cent by volume (Sollmann, 1939).

The concentration of ether in blood in different stages of anæsthesia has also been worked out. Edmunds and Gunn (1936) give the following figures: a concentration of 100 to 110 mg. of ether per 100 c.cm. of blood produces light anæsthesia, one of 130 to 140 mg. produces deep anæsthesia, while one of 160 mg. or more produces a fatal result.

Limits of explosibility of ether vapour

The vapour of ether like all other inflammable gases and vapours must be present in air in a certain minimum proportion before it becomes explosive. Below this minimum limit, the mixture, on account of its dilution with too much air, cannot be ignited. There is moreover a maximum, beyond which the mixture again becomes inexplorable, although it remains inflammable and on ignition gives a flash (von Schwartz, *loc. cit.*). This is due to the presence of much excess of ether vapour, much more than is necessary to produce an explosion, and so it burns quietly. There is, however, much divergence of opinion about these two limits, and no two authors agree on the exact limits of inflammability or explosibility of ether-air mixtures. Bunte (von Schwartz, *loc. cit.*), who has worked out the limits of various gases and vapours ignited by electric sparks, gives a range of 2.9 to 7.5 per cent by volume of ether vapour in ether-air mixtures. - Coward and Jones (1931)

of the U.S. Bureau of Mines give a much wider range, *viz.* 1.7 to 26.0 per cent by volume, but the method of ignition was not recorded by them. Von Schwartz (*loc. cit.*) stated, after a perusal of the literature on this subject, that 6 per cent by volume of ether vapours in air is the upper limit for explosion—the lower limit as well as the method of ignition not being stated by him. Beilstein (*loc. cit.*), on the other hand, quotes authorities to show that 4 per cent is the optimum concentration, while the range is 1.8 to 6.0 per cent by volume, and Jacobs (1941) gives a range of 1.8 to 36.5 per cent by volume. We have found by experiments that the lower limit of ignition (with a burning match stick) is about 2 per cent by volume, that is, practically the same as that quoted by Beilstein and by Jacobs (*loc. cit.*).

It may, however, be noted that laboratory experiments with pure gases, and vapours contained in glass jars and flasks, are in no way comparable to the conditions prevailing in an operation theatre where there are many extraneous factors to modify the experimental results. In a room with closed doors, with half a dozen or more people working, and one or more powerful kerosene lamps burning, the atmosphere necessarily becomes charged with CO_2 and moisture, produced mostly by the burning lamps and partly by the occupants, to such an extent as to reduce considerably the explosibility of the ether-air mixture, and to raise its lower limit much above those calculated by different observers.

Taking these facts into consideration, it may be stated that the lower limit (2 per cent) as obtained by laboratory experiments with pure vapours is far too low and not applicable to conditions obtaining in operation theatres. Since the smell of a mixture containing 5.6 per cent of ether vapour in air (the usual concentration for anæsthesia) is unpleasant and suffocating, it is unlikely that a 2 per cent mixture will not be so unpleasant as to remain undetected by those accustomed to the smell of ether, and it has been actually found that even a 1 per cent mixture cannot be tolerated for any length of time.

Possibility of ether fires in operation theatres

As the presence of 5.6 per cent of vapour in air produces anæsthesia, it is not possible to work in such an atmosphere. In operation theatres where a large number of operations are performed continuously under ether anæsthesia, neither the surgeons nor their assistants, however, feel any uncomfortable sensation due to ether. This shows that at the level of the surgeons' head, the concentration of ether vapour is negligible, and at a level higher than this, that is, where the lamp is suspended, there is perhaps no ether at all. But it may be contended that as ether vapour is heavier than air, it settles at the floor, and the concentration there may reach the dangerous limit without being detected by the occupants, and if, at this stage, the lamp is

placed on the floor for pumping or refuelling, it may ignite the ether-air mixture and produce a flash or an explosion. Theoretically, this is undoubtedly possible, but a consideration of the following facts indicates that this possibility is a remote one :—

(1) The movement of the persons working in the operation theatre disturbs the stream of vapour pouring down from the operation table and scatters it in all directions.

(2) After each operation the activities of the assistants in removing the patient and bringing in another one, accentuate further the dilution and dispersal of ether vapour and its exit through open doors.

(3) High temperature inside the room helps the dilution and flowing out of ether vapour through the chinks of closed doors and windows.

(4) The CO_2 gas formed there also sinks down to the floor level but, being more diffusible than ether vapour, gets mixed with the latter more readily and produces its inhibitory action.

(5) The atmosphere in immediate contact with the lamp is so rich in CO_2 that the ether-air mixture, unless it is a very strong one (which is improbable under the circumstances), is likely to be admixed with excess of CO_2 and thereby rendered innocuous.

(6) The amount of moisture already present in the room and subsequently enhanced by respiration and combustion, also exerts considerable inhibitory action.

(7) As the vapours of ether are very easily decomposed by heat, yielding formaldehyde, etc., the hot metal parts of the lamp tend to prevent the concentration of ether (if not already an explosive mixture) from reaching the dangerous limit near the lamp.

Summary and conclusion

The facts discussed in the foregoing pages indicate that the concentration of ether vapour at the height at which the lamps are usually suspended is practically nil, while the concentration even on the floor, where the lamps may be placed for purposes of refuelling or pumping, is not expected to reach even a small fraction of the proportion necessary for its ignition. There is, however, no rapid and reliable chemical method for determining the quantity of ether vapour present in the air of a room, and the surgeon has, therefore, to fall back on his sense of smell and to compare the intensity of the smell in a particular place with that of the concentration (7 per cent) in the mask which produces anaesthesia and with which the surgeon and his assistants are so familiar.

Since ether vapour is highly inflammable, and ether-air mixtures in certain proportions are explosive, and as accidents do happen in laboratories and explosive factories in spite of taking precautions based on all theoretical calculations, surgeons should always remember that proper ventilation in the operation theatre is of supreme importance to the prevention of ether fires, and

this is effected best by installing exhaust fans at the floor level. If this is not feasible, the use of large hand fans after each operation with the doors and windows opened out, may serve the purpose. The pumping, cleaning or refuelling of the petromax, or any other open lamp should be done on a high stool (about 3 feet in height) and not on the floor where ether vapours are likely to accumulate. The swabbing of the floor with wet jute swabs at frequent intervals or after each operation, is also very helpful in dispersing ether vapours from the floor and keeping down or removing the dust particles which otherwise create trouble.

Acknowledgments

I am indebted to Major-General W. C. Paton, I.M.S., Surgeon-General with the Government of Bengal, at whose suggestion this study was taken up.

I must thank Mr. Annada Bhattacharjee, Officiating Assistant Chemical Examiner, for his keenness in carrying out the risky experiments with explosive mixtures.

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Medical News

INDIAN CHEMICAL MANUFACTURERS' ASSOCIATION

THE Committee of the Indian Chemical Manufacturers' Association met Mr. Ram Chandra, the Chief Controller of Imports, at the premises of the Association when the difficulties experienced by the Chemical and Pharmaceutical Works for importing essential raw drugs, medicines, etc., were discussed. The Chief Controller stated *inter alia* that the Government did not consider only those drugs and medicines useful for war purposes as essential, but also included civilian needs under the category of 'essential' drugs and medicines. He has assured the Association that essential drugs and medicines required by the manufacturers in the country for civilian needs will always

receive the immediate attention of the Government. The Chief Controller of Imports has further stated that the Government will be willing to give necessary permits for importing quinine from foreign countries provided the latter are prepared to allow its export. The Committee also referred to the necessity of allowing import of codein and other opium alkaloids from the United States of America and United Kingdom.

SIR HENRY DALE, P.R.S.

Sir Henry Dale has just accepted the chairmanship of the Science Committee of the British Council.

Sir Henry is the President of the Royal Society of London and Director of the National Institute of Medical Research. He has shared a Nobel Prize for Medicine with Professor Loewi for his elucidation of the way in which nerves act. In 1921, Loewi published evidence that nerves exert their effects by the release of chemical agents. Dale immediately suspected that these agents were adrenaline and acetylcholine. By 1929, in collaboration with Dudley, he had confirmed that acetylcholine was indeed one of the agents, and Loewi proved later that the other was adrenaline. It seems that all motor nerves in mammals produce their effects by the local liberation of one or other of these two substances.

Dale has accomplished many researches on other agents that have an important rôle in the body, such as histamine, which is connected with shock.

His colleagues at the National Institute of Medical Research have made a series of discoveries concerning hormones, vitamins, influenza viruses, and other fundamental agents.

The Institute is also the centre for biological standards. Representative samples of many of the newly-introduced medical agents, such as sex hormones and vitamins, are kept there. The strength of the specimens used by doctors and research workers is measured by comparison with these samples, so that the new drugs can be used according to an exact and uniform system of doses, and thus prevent any confusion.

TRANSFUSION FLUIDS FOR MATERNITY CASES

The Ministry of Health, London, has issued a circular concerning the revision of arrangements for supplying maternity units with transfusion fluids and apparatus for transfusion from the Emergency Blood Transfusion Services.

Arrangements of this kind appear to be a permanent feature of the work of maternity services.

AUXILIARY NURSING SERVICE, INDIA REVISED SALARY SCALES

The Government of India are revising the conditions of service for the members of the Auxiliary Nursing Service, India (General Service). In addition to free board (rations, messing and mess servants) and lodging (accommodation, furniture and light), the rates of pay will now be Rs. 100-2½-120-3-126 for the Uncertificated Auxiliary Nurses. All members who join the Army after the introduction of the new terms will be governed by them; existing members will have the option of electing to remain under the old terms if they so desire in which case they will be required to pay full messing charges. Having once elected to be governed by the revised terms, a member will have no right to revert to the old rates of pay.

SPECIAL I.M.S. COMMISSIONS FOR SERVICE IN INDIA

The Government of India have decided to open recruitment to Emergency Commissions in the Indian Medical Service for service within Indian limits, to specialists possessing appropriate post-graduate medical qualifications and sufficient experience in the special

subjects of Medicine, Surgery, Ophthalmology, Diseases of Ear, Nose and Throat, Dermatology, Mental Diseases, Gynaecology, X-Ray and Anæsthetics. Officers recruited in this category will be granted a lower rate of pay than specialists recruited to the general service cadre of the Indian Medical Service, but their other terms and conditions of service will generally be the same as for the latter. These officers will be commissioned as Lieutenants in the first instance, and will subsequently be granted the acting rank of Major when holding specialist posts.

They will be exempted from preliminary military training.

INDIAN MEDICAL COUNCIL

In exercise of the power conferred by clause (a) of sub-section (1) of section 3 of the Indian Medical Service Act, 1933 (XXVII of 1933), the Central Government is pleased to nominate Major A. N. Chopra, M.B., B.S. (Pb.), N.T.M. (Liv.), D.P.H. (Eng.), I.M.S., Director of Health and Inspector-General of Prisons, Orissa, to be a member of the Medical Council of India, from Orissa, with effect from the 1st March, 1943, vice Lieut.-Colonel G. Verghese, I.M.S., resigned.

THE FACULTY OF TROPICAL MEDICINE AND HYGIENE, BENGAL

The following students are declared to have passed the D.T.M. Examination, Session 1942-43.

Passed with distinction

1. Dr. Manohar Prakash Ranbise, L.C.P. & S. (Bom.), Demonstrator, Miraj Medical Centre—Awarded the 'Chuni Lal Bose' Gold Medal, 1943.

Passed

- (Arranged in alphabetical order)
2. Dr. Janki Prasad Bhargava, M.B., B.S. (Bom.), medical officer, Gwalior State Service.
3. Dr. (Miss) Bimala Bhattacharya, M.B. (Cal.), house medical officer, Eden Hospital, Calcutta.
4. Dr. Satya Charan Bhattacharyya, M.B. (Cal.), medical officer, Anglo-India Jute Mills, Jagatdal.
5. Dr. Satyabrata Chatteraj, M.B. (Cal.), private practitioner.
6. Dr. Cheng-I Wang, M.D. (Peking Union Medical College, China), Medical Service, Government of China.
7. Dr. Chapala Nath Choudhury, L.M.F., L.T.M. (Cal.), private practitioner.
8. Dr. Bijoli Bhushan Das, L.M.F. (Cal.), private practitioner.
9. Dr. Bishnu Pada Das, L.M.F., M.B., D.P.H. (Cal.), medical officer and health officer, Dum Dum municipality.
10. Dr. Gopal Chandra De, L.M.F., L.T.M. (Cal.), private practitioner.
11. Dr. Murari Mohun De Sarkar, M.B. (Cal.), house surgeon, Medical College, Calcutta.
12. Dr. Harisadhan Ghosh, M.B. (Cal.), house surgeon, Carmichael Medical College Hospitals, Calcutta.
13. Dr. Damodar Dhondji Jarare, M.B., B.S. (Bom.), medical officer, Gwalior State Service.
14. Dr. Sital Das Nandy, M.B. (Cal.), private practitioner.
15. Dr. Indu Bhushan Roy, L.M.F. (Assam), L.T.M. (Cal.), medical assistant, Assam Medical Research Society, Shillong.
16. Dr. Siba Das Sarkar, L.M.F. (Bengal), medical officer, Khalsini Charitable Dispensary, Chandernagore.
17. Dr. Rabindra Nath Sil, M.B., B.S. (Rangoon), private practitioner.
18. Dr. Tan Eng Gwan, M.B., B.S. (Hongkong), private practitioner.
19. Dr. (Miss) Winifred Williams, M.B., B.S. (Lady Hardinge Medical College, New Delhi), Women's Medical Service Training Reserve.

Current Topics

Bacteriostatic Effect of Sulphathiazole in Ointment Bases

By STRAKOSCH

and

OLSEN

(Abstracted from the *Archives of Dermatology and Syphilology*, July 1942)

THE management of streptococic and staphylococic infections of the skin presents an important problem. The authors reported studies on the bacteriostatic action of 5 per cent sulphathiazole in thirteen different ointment bases. They employed blood agar plates which were closely streaked with *Staphylococcus aureus* and beta hæmolytic streptococci from a twenty-four hour broth culture. Slightly warmed ointment was applied on the plates by means of an eye dropper in amounts of 0.3 gramme. After application of ointment the plates were incubated upside down at 37°C. The plates were examined after six, twelve, twenty-four and thirty-six hours. The width of the zone of the inhibition was measured with a millimetre rule under a hand lens. Similar ointments were made with sulphanilamide. The observations allowed these investigators to conclude that when sodium sulphathiazole is incorporated into suitable ointment bases it does not lose its bacteriostatic power. Sodium sulphathiazole is most rapidly effective when incorporated into bases of the water in oil type of emulsion which are rich in cholesterol, and it is likewise in these bases that the maximum effect was noted; and finally it appears that the relative mixture of fats and the emulsifiers in the fats of the base are of chief importance in liberating the incorporated drug.

Human Plasma in Spinal Anæsthesia

By E. M. PAPPER

and

E. A. ROVENSTINE

(Abstracted from the *Journal of the American Medical Association*, 15th August, 1942)

THE two most important problems concerning the use of spinal anæsthesia are the preferred technique necessary to produce the desired extent of anæsthesia in a manner predictable and with minimal dangers and to secure the desired duration of anæsthesia with doses of the agent that provide a wide margin of safety. As a contribution to this subject, the authors report studies on 5 normal male volunteers, employing human plasma as the solvent for the procaine employed in spinal anæsthesia. The technique was standardized as far as possible. A level table was used. Lumbar puncture was performed in the fourth lumbar interspace with the subject lying on his left side. The dose of procaine selected (3 subjects were given 100 mg. doses and 2 were given 50 mg. doses) was then dissolved in 2 c.c. of spinal fluid or 2 c.c. of plasma, and injection was completed in exactly ten seconds. The subject was turned gradually and gently to the supine position. The sensory level of anæsthesia was noted at frequent intervals by response to pinprick, and motor power of the lower extremities was observed at the same time. Two end points with regard to sensory anæsthesia were noted: the beginning of recession from the maximum height and the ability to perceive painful stimuli at the level of the twelfth thoracic vertebra. The return of motor power was indicated by any motor activity of the lower extremity. This technique was later employed for clinical anæsthesia on 70 patients. The majority of

the latter were subjected to surgical procedures in the lower part of the abdomen and lower extremities. There have been no untoward manifestations during surgery or postoperatively that might be attributed to the plasma. Observations of these few cases have left the impression that dose for dose the duration of procaine spinal anæsthesia is prolonged when plasma rather than spinal fluid is the diluent. Predominantly, motor or sensory anæsthesia can be obtained easily and as desired by appropriate adjustments of the position of the patient.

Desoxycorticosterone Acetate for Epileptic Seizures

By I. McQUARRIE

J. A. ANDERSON

and

M. R. ZIEGLER

(Abstracted from the *Journal of Clinical Endocrinology*, June 1942)

THE authors determined the effects of desoxycorticosterone acetate on the water and electrolyte exchanges and on the occurrence of *grand mal* seizures in two severely epileptic patients. They found that this synthetic cortical adrenal hormone effectively antagonized not only the electrolyte responses, but also, under the conditions represented in these experiments, the seizure-provoking effect of the anti-diuretic posterior pituitary hormone (pitressin). Preliminary therapeutic tests indicated that desoxycorticosterone decreases the tendency to spontaneous occurrence of *grand mal* seizures, also. The results presented tended to confirm an earlier conclusion regarding the nature of the convulsive mechanism in genuine epilepsy. Possible dangers from prolonged, indiscriminate administration of desoxycorticosterone acetate contra-indicate its use until further investigations now in progress have been completed.

Modern Microscopy

(From the *Medical Press and Circular*, Vol. 208, 16th September, 1942, p. 179)

WERE Leeuwenhoek to return to-day, he might find the latest developments in the science which he founded rather beyond him, unless he were given a reasonable interval in which to adjust his ideas to the new conceptions in the vast and complex field of modern physics. For the latest developments in microscopy dispense with light altogether and employ instead those electrons which, according to modern theories, are the bricks out of which the atoms of matter are built. Sometime before the outbreak of war a few meagre details of this development had just begun to filter through to our daily Press, although some five years previously, a good account had been published in a contemporary British scientific journal. In the current number of *Chemical Products*, Professors Marton and McBain, of Stanford University, California, give a very good outline of the principles on which the electron microscope is based and the way in which it can be used. Certainly it is one of the most fascinating developments in the whole field of modern science and while it must be remembered that it is still in its early infancy, it has already given more than a hint of the vast potentialities which lie before it.

Electrons versus light

The principle on which it works is based on the fact that the electron, while for some applications behaving as a corpuscle, for other applications 'behaves as a wave, whose wave-length depends on the speed of the electron and, for the speeds at present used in electron microscopy, it is about one-100,000th of the wave-length of visible light. Under identical conditions this would mean 100,000 times better resolving power,

or 100,000 times higher useful magnification with the electron microscope than with the light microscope. This, however, cannot be fully realized, the limitations being largely due to aberrations of the lenses'. Few can doubt that these aberrations will in time be corrected; in the meantime the magnification—some 25,000 times greater than that of our best oil-immersion lenses—which it puts at our disposal would seem to be sufficient for the moment.

Power and flexibility

The instrument itself looks rather like one of our standard light microscopes, except that it is about twenty times larger, and inverted so that the observer sits at the base. The actual construction is curiously like that of an ordinary microscope, being based on the fact that a stream of electrons can be concentrated by a magnetic field in the same way as a lens concentrates a beam of light. The 'lenses' referred to above are really coils through which a current is flowing. Any object which interrupts the stream of electrons will form an image which can be projected on to a fluorescent screen or photographed. Focusing is carried out, not by moving the coils about, but by varying the strengths of the electrical fields, so that any magnification from the highest to the lowest can be obtained without any other adjustment. Since the electron stream will only flow readily in a vacuum, the whole instrument must be fairly completely exhausted. This, together with the fact that the electrons must travel at voltages varying from 30,000 to 100,000, suggests that most of us will have to be content with our present microscopes, at any rate for some time to come.

Prospects unlimited

There is no doubt that in the years to come this instrument should enable us to clear up most of the mysteries which at present so mightily perplex us, apart from the new discoveries which are bound to flow from it. Already a number of varieties of virus have been examined and there would seem to be no good reason why the appearance of all such pathogens should not become as familiar to us as their larger associates the cocci, the bacilli and so on. Again antibody-antigen reactions have been observed while actually taking place. Already, indeed, it is believed that the actual molecules can be seen and the effort will no doubt be sustained until resolution is brought down to atomic dimensions, thus embracing all matter. The implications of this so far as, say, histology, hæmatology and pathology are concerned should be obvious. In any event the term 'ultramicroscopic' should pass out of scientific language, a development which we can afford to contemplate without regret. And a new chapter of unimaginable splendour in the history of science seems to have begun.

The Modern Treatment of Alcoholism

By ALFRED E. CARVER, M.D., D.P.M.

(From the *Medical Press and Circular*, Vol. 208, 4th November, 1942, p. 295)

ALCOHOLISM is the oldest and most widespread of all addictions, yet its treatment, like that of the common cold, leaves much to be desired. Research, however, continues and new approaches constantly are being introduced, many of which have advantages, so long as basic principles established by past experience are not overlooked.

If for a moment we disregard the student type of drinker, who to celebrate some college rag indulges in a rare 'binge', we may define an alcoholic as a person who cannot face reality without alcohol, and whose adjustment to reality is impossible so long as he continues to take alcohol. Our essential task is to combat the basic instability of the addict, not simply to detoxicate him, or to remove alcohol from his reach, or to make alcohol itself distasteful to him. Detoxication is easy, but readjustment of the patient against risk of

relapse is among the most difficult tasks of medicine. In addition we have to deal not only with its original motivations, but with a habit, the establishment of which has secondarily affected both behaviour and tissue reactions. It is, however, impossible to lay down any hard and fast line the crossing of which justifies classification as an addict. The make-up and susceptibility of individuals vary greatly, and within wide limits the quantity of alcohol consumed affords no criterion, e.g. persons who have suffered from concussion or head injuries are notoriously hypersensitive. There is, nevertheless, sufficient correlation between the percentage of alcohol in the blood and the behaviour of the drinker to justify the new law in Sweden, which provides that an alcohol content in the blood of 1.5 per 1,000 shall of itself be accepted as sufficient proof of unfitness to drive.

Let us first consider the treatment of acute alcoholic intoxication, then the treatment of alcoholic addiction whether regular or intermittent. Space does not permit a consideration of sequelæ, which also is unnecessary here, as the treatment of these conditions is independent of their alcoholic causation.

A doctor usually is called when the patient is suffering from acute intoxication. It is important that he satisfy himself as to the correctness of the diagnosis and bear in mind the fact that evidence of recent imbibition of alcohol does not prove that the patient's symptoms are due to this alone. Once the diagnosis is established the first step is to empty the stomach. A large size stomach tube is most convenient for the purpose and the method has the advantage that the organ can be thoroughly washed out, also that in debilitated persons a pint of hot coffee can be introduced when the lavage is completed. An easier and more drastic method is the subcutaneous injection of apomorphine gr. 1/20 to gr. 1/10. This causes vomiting and is followed immediately by sleep lasting two hours or more. The method is excellent for robust and rowdy patients. Care should be taken not to leave the patient until vomiting has ceased, lest in his sleepy condition vomited material choke him or be insufflated.

For what has been termed the student type of 'binge', further treatment probably will not be needed. There is, however, the question of 'hangover', and recent work done in America shows that intravenous injections of cardiazol (5 c.c. of a ten per cent solution) have a steadying effect upon the acutely intoxicated. It has also been found that injections of insulin and glucose accelerate the elimination of alcohol from the blood, but this is better left for practice in institutions.

The next question which arises is whether alcohol shall be cut off abruptly or withdrawn by tapering. The general consensus of opinion is that, except as a placebo, alcohol should be cut off abruptly in all cases except elderly, long-addicted patients, and even in them the tapering process should be accomplished in less than a week. Daily reduction should be by one-third the previous amount until the dose falls to about 6 ounces at which it is discontinued. Addition of paraldehyde to the whisky used for tapering has a threefold advantage: (1) it renders the dose unpalatable, (2) it prevents the patient from knowing how much whisky his dose contains, and (3) last but by no means least, it has a powerfully soothing action, which is a great desideratum at this stage of treatment.

Once the detoxication stage is over it becomes important to decide whether further treatment is required and if so under what conditions. Experience has shown that the good will and co-operation of the patient himself are essential, also that treatment must be carried out under special conditions not in the patient's own home or even in an ordinary nursing home. It is a great advantage if the doctor understands the reason for this, is able to persuade his patient to undergo adequate treatment and then keep an eye upon him when he returns home.

In a special institution the various factors entering into a course of treatment can be brought to bear concurrently while the patient temporarily is removed from the environment which prompted recourse to alcohol. A regulated life, therapeutic occupation, and

medicinal measures proceed *pari passu* with the even more important psychological treatment. The latter cannot be discussed here, but its aim is to give the patient an insight into the motivations which underlie his flight to alcohol and then to get him to readjust himself. Unless this can be achieved relapse is probable. During the first day or two, diet should be light, nourishment of the egg-flip type being given three-hourly until the patient is fit for ordinary food. Of recent years it has become routine practice to give vitamin B in all cases of alcoholism, though its use is particularly indicated in cases of delirium tremens, polyncuritis and Wernicke's syndrome. It may be given parenterally in the form of thiamin-chloride or one of the many proprietary preparations. Also by mouth as yeast, bemax or marmite.

Alcoholism is associated with impaired sugar metabolism. Within limits alcohol can replace sugar, but it cannot be stored or converted and must therefore be oxidized immediately, otherwise the excess will remain as a poison in the system. Alcoholists seem to have the bad habit of attempting to replace sugar by alcohol. Hence when alcohol is cut off sugar must be substituted. At first glucose may be given by intravenous injection or by mouth. Later the patient develops a taste for sweets and should be encouraged to eat small quantities of block chocolate in the middle of the morning and afternoon. It is surprising how satisfactory a small dose of sugar in this way relieves a jaded feeling and prevents the development of a desire for alcohol as a pick-me-up. Dr. Horace Hill has recently advocated treatment of alcoholism with injections of histamine and insulin. The dosage is below that required to cause convulsions, and the technique is simple, yet the method should only be carried out in an institution with properly trained staff. It does mark an advance in that it attempts a radical change in certain metabolic disturbances associated with and probably conducive to alcoholism.

In the early stages of treatment, alcoholists generally require sedatives. Fortunately a number of suitable ones are at our disposal, *e.g.* members of the barbitone and carbamide groups as well as such old friends as chloral and bromide.

The use of paraldehyde in tapering has already been referred to, but its continued exhibition should be avoided. Its pungent smell cannot be disguised and the patient soon finds out what it is and can get it for himself upon some future occasion. In the writer's opinion a patient should not be allowed to know what sedative he is having; also, in order to avoid risk of habituation, it should frequently be changed.

Apomorphine, which already has been recommended for its emetic properties in acute intoxication, has other important uses. In small repeated doses (gr. 1/40 subcutaneously) it is often efficacious in warding off a threatened relapse in a dipsomaniac. Small doses are calming and do not cause vomiting. A single dose gr. 1/30 given last thing in bed is an excellent remedy for insomnia of the delayed type.

Apomorphine has also been used in an attempt to 'contra-condition' the addict to alcohol. Recently this method combined with vigorous suggestion has been favourably reported upon by Voegtlin in U.S.A. The rationale of the method is based upon Pawlow's work and seeks to associate the unpleasant effects of apomorphine with the taking of alcohol. Emetine may be used in the same way, but the writer does not favour these methods because they attack alcoholism as a symptom without seeking to readjust the underlying instability of the patient.

Of recent years benzedrine has been experimented with in alcoholism and in neuroses. Various claims have been made for it, which in the writer's opinion are not borne out in practice. Its action resembles that of cocaine, the gap between therapeutic action and toxicity is narrow, and the development of addiction a real danger. These facts are worth recording because the writer has come across cases where benzedrine was being substituted for alcohol and was proving a worse master. The fact that when neurotics, who have become addicts, meet with any check in procuring their

original drug of addiction, they readily turn to another, should be ever present in the minds of everyone treating them.

While the course of general and psychological therapy is proceeding, empirically it has been found helpful to give hypodermic injections of strychnine and atropine. The technique is as follows: A solution of strychnine gr. iv to 3i of sterile normal saline in a rubber-capped vial. Also a solution of atropine sulph. gr. i to 3i in another vial. The injection is given subcutaneously over the deltoid region after meals. Begin with m. ii of each solution and increase gradually until at the end of a month or more the dose reaches m. vi of each, at which level it is held for a week or two and then gradually reduced. During this period the following tonic is usually given by mouth before meals:—

Inf. cinch. acid con.	3i
Tinct. capsici	m. ii
Aq. chlorof. ad.	3i

In lieu of the injections above described, tinct. nux vom. and tinct. belladonnæ may be added to the tonic mixture in gradually increasing doses as tolerance rises. In this case the mixture is better taken after meals. Experience has shown that in order that there may be reasonable chance of establishing a permanent cure, the duration of stay in the special institution should be not less than three months.

Prognosis depends upon (1) mental make-up of the patient, (2) the depth of the unconscious motivations for recourse to alcohol, (3) duration of excess, (4) presence or absence of incentives to rehabilitation. The greater the deviation from the normal of any or all of these factors the more gloomy becomes the outlook.

It is of the greatest importance that a person who has once displayed hypersusceptibility to alcohol should realize that this entails abstinence. The only safe course for the susceptible is that henceforth for ever he remains a total abstainer. A great many of those who enter a special institution for treatment have already discovered for themselves, and much to their chagrin, that they cannot play with alcohol, or for long remain moderate drinkers. Others, however, in spite of personal experience to the contrary persist in hoping that they will be all right if they stick to beer, they are reluctant to realize that for the person who has shown susceptibility the reaction is of the all or none type and that once they begin again it is only a matter of time before excess is reached. The ban must therefore be placed against the 'fatal first drink'. Only by the observance of this restraint can such persons avoid relapse.

Upon discharge, all patients should go direct to work, any idle interval is to be avoided. With many, especially those of weak will and convivial inclination, it is advantageous that arrangements be made for them to keep for a time in close touch with the family doctor. The latter from his intimate knowledge of the patient's environment may be able to suggest helpful little modifications in it, and to put in the right word with friends and family. It has often been found that a course of emetine hydrochloride injections is helpful at this period. A sterile solution of emetine hydrochloride gr. 1 to 1 c.c. is made up in a rubber-capped phial and 3 c.c. injected every other day. During his visits for a short course of injections the patient can be fortified in his resolution to remain a total abstainer and recommended to attribute being on the water wagon to medical advice that alcohol is injurious to his kidneys or other organ, as this prevents his so-called friends from attempting to persuade him that 'another little drink won't do him any harm'. After a short time his status as a teetotaler becomes accepted and he escapes the temptation of trying to be a moderate drinker in order to please his friends. Thus in many ways the G.P. can exercise a helpful influence in relaunching his patient into the world.

Alcoholism has shared with cancer and tuberculosis an extensive advertising campaign by proprietary and secret remedies, some of which claimed to be efficacious even when administered in the victim's food all unbeknown to him. It should be needless to warn

members of the medical profession against such easy magic. The writer, however, has come across instances where doctors rather despairingly have yielded to the importunity of a difficult patient's relatives. Thus perhaps acceptance of a more genuine and rational effort to attain a cure has been postponed or lost.

The present time calls for a postscript upon 'Hooch', or, in other words, methyl alcohol. This is consumed by impecunious addicts generally as 'Red Biddy', or accidentally by those indulging in bootleg spirits adulterated with methyl. Methyl alcohol cannot be oxidized in the system to form CO_2 and water, but is slowly transformed into derivatives of methane, which cause acidosis. Usual symptoms are depression, severe pains in the head and stomach, vomiting and cramps, loss of vision, rigidity of pupils and failure of circulation and respiration. Occasionally violent maniacal behaviour is displayed. Treatment, after washing out the stomach as already described, is directed against the acidosis by large injections of 5 per cent sodium bicarbonate solution and stimulation by analeptic drugs. Laboratory experiments suggest that the toxicity of 'Hooch' is not entirely attributable to methyl alcohol itself but to impurities commonly contained in it. The prevalence of 'Hooch' poisoning is increased when for any reason ordinary ethyl alcohol drinks are more than usually difficult to obtain, as is now the case owing to war.

The Hazards of Transfusion

By L. E. H. WHITBY

(Abstracted from the *Lancet*, Vol. I, 16th May, 1942, p. 581)

THE author, who is Consulting Physician in Blood Transfusion and Resuscitation to the British Army, recently delivered the text of this paper at a meeting of the Harveian Society of London.

He places the hazards of transfusion in four categories: (1) the systemic type of reaction, particularly associated with the crystalloid fluids; (2) circulatory disasters due to the general condition of the patient; (3) intravascular hæmolytic; ordinarily concerned with questions of incompatibility of the blood being administered and (4) diseases transmitted from donor to recipient.

SYSTEMIC REACTIONS

Reliable statistics concerning reactions of this type are difficult to obtain because the incidence varies with the person giving the transfusion, the method employed, the rate of administration, and the condition of the patient. Too fast a rate is a common cause of rigor. Most authorities now agree that with stored blood cleanly and properly taken, the incidence of reactions is no greater than with fresh blood, provided that the blood is not more than three weeks old. Pyrexial reactions are mainly due to foreign protein, either dead bacteria or even living non-pathogenic bacteria which might be found in stale distilled water. It is better to make up the intravenous solutions with good fresh tap water than with stale distilled water, because the bacterial content of the former is much lower. The most important differentiating feature between a pyrexial reaction due to bacteria or some foreign protein and the reaction which indicates intravascular hæmolytic from incompatibility is that true incompatibility is almost always associated with violent lumbar pain occurring instantaneously.

CIRCULATORY DISASTER

Crystalloid solutions leave the circulation even though blood volume is reduced. Their proper use is for the treatment of tissue dehydration and not for their fleeting effect on blood volume restoration. On the other hand, water which is bound to protein, as in blood, serum, or plasma, is retained in the circulation if blood volume is reduced, and, if excreted, it does not follow the same path as water bound to a crystalloid. Transfusions under war conditions have to be of a massive order—5 to 7 pints (2.8 to 4 litres)

of blood or blood substitute—and there is danger of overloading the circulation. An analysis of 6 transfusion fatalities in peace-time showed that, in 4, the deaths were due to pulmonary cedema, but that these were people with enfeebled cardiac muscle. It can be assumed that the ordinary casualty in war has a normal cardiac muscle before being wounded; from an experience of 150 transfusions in casualties, the author has not seen one case of pulmonary cedema from necessary massive transfusion. Failure to restore blood volume is a much greater danger.

INCOMPATIBILITY

The question of incompatibility grows more confused every day. The hazard to be faced with gross incompatibility is agglutination and lysis of the cells, leading sometimes to immediate death, but death is by no means inevitable. Landsteiner group compatibility depends upon proper serum for carrying out group tests. The greatest danger is the use of an impotent serum. Infected testing serum also gives rise to considerable difficulty because it has pan-agglutinating properties. Cold agglutination—agglutination which occurs only below body temperature—gives rise to the same kind of result.

The author then discusses the degree of safety of 'universal donors', emphasizing the great importance, especially in repeated transfusions, of performing a direct grouping test properly, and also of the simple biological test, the slow injection of the first 20 c.cm. of the transfusion, and the fallacy of assuming that the once compatible donor would always be compatible to the same recipient. He also refers to the prominence recently given to the rhesus (Rh) factor. Ideally, Rh-negative donors should be used, but otherwise relative security can be obtained with the direct grouping test and the simple biological test. The Rh factor has been used to explain the hæmolytic tragedies of birth—erythroblastosis foetalis and icterus gravis—and is probably the explanation of most of the hazards which have been previously attributed to Group O donors.

TRANSMISSIBLE DISEASES

In disease transmissible from donor to recipient, syphilis comes first to mind but the risk in Britain is not great. Up to the time of war, about 40 cases of transmitted syphilis had been reported in Britain and North America. The usual safeguard is a serological test of the donor, but the limitations of that safeguard should be appreciated. The late primary and early secondary stages of syphilis are the most infectious, but, in these, the serological test is often negative, or at least doubtful, whereas with a good tertiary there would be a positive serological test and yet the individual might be quite innocuous as a donor. Storage of blood affords a considerable protection against syphilis, because the spirochæte appears to survive only five days in the refrigerator.

There have been practically no reports of the transference of virus infections from stored blood. Malaria is a hazard difficult to avoid, and it is not known how long the parasite survives under refrigerator conditions. Allergy to proteins might be transmitted, as a rule lasting for only a few weeks.

The author concludes by saying that the majority of transfusion hazards are avoidable. The simple pyrexial ones can be eliminated by scrupulous cleanliness; practical experience and clinical judgment reduce the incidence of circulatory disasters, while intravascular hæmolytic from incompatibility will always occur from time to time, but mainly as the result of improper performance of grouping tests.

Acute Intestinal Obstruction from the Clinical Standpoint

By K. P. BROWN

(Abstracted from the *Edinburgh Medical Journal*, Vol. XLIX, April 1942, p. 234)

THE author's purpose in writing this paper has been to consider certain physiological facts, to discuss how

the physiology is modified by various forms of post-operative intestinal obstruction, and so to be in a position to describe a rational form of treatment based on these facts.

In both high and low obstruction of the small intestine, large quantities of water are lost, in the former by vomiting and in the latter mainly by increasing fluid distension of the bowel. This dehydration is one of the essential effects of intestinal obstruction, and in terms of actual volume of water lost may mean that a patient has lost at least 6 per cent of his body-weight in water alone. Chloride loss is of equal importance, but is of greatest significance in the presence of a high obstruction, when the plasma chloride concentration may be very markedly reduced.

It has been estimated that a surgical patient requires 2,000 c.cm. of water daily in addition to 1,500 c.cm. of water for the urine. Thus in the presence of an intestinal obstruction, where large quantities of water may be lost, these losses must be replaced in addition to the daily allowance of 3,500 c.cm. Sodium chloride must similarly be replaced. In a normal person, about 6 grammes of salt are required daily, but if the salt intake be stopped and chlorides be lost by vomiting, intestinal fistulae, etc., the plasma chloride concentration falls below the normal figure of 560 to 650 mg. per 100 c.cm., and hyponatraemia results. It is stated that from 15 to 20 grammes of sodium chloride are required for every 100 mg. that the plasma chloride concentration is below normal.

Dehydration and hyponatraemia can be corrected by the intravenous administration of saline, but salt depletion may be overcome before enough water has been given to stabilize the water balance. If the total quantity of fluid required is given in the form of saline, the patient will receive an excess of salt. This excess raises the osmotic pressure of the extracellular fluid, resulting in the transference of more water into this fluid and the production of clinical oedema. It is, therefore, most important that, when salt depletion has been corrected but more water is required to control dehydration, it be given in the form of 5 per cent glucose solution in distilled water.

CONSERVATIVE TREATMENT OF INTESTINAL OBSTRUCTION

This method is employed mainly in the treatment of paralytic ileus. In those cases where an ileus may be expected to develop, preventive measures can be adopted. A patient with gangrenous appendicitis and early peritonitis is given 1 c.cm. of pituitrin at four-hourly intervals, commencing immediately after operation. If an ileus already exists, all intestinal stimulation is avoided, 10 mg. morphine is given frequently, and gastro-duodenal suction, by means of a tube passed through the nares, is commenced. This suction is continued until abdominal distension is relieved and the aspirated material is no longer dark and foul-smelling. All the aspirated fluid must be measured, as a balancing quantity of saline has to be given intravenously in addition to the necessary water to maintain a normal fluid balance.

When a mechanical obstruction exists, conservative treatment is sometimes successful and is always helpful in rendering the patient better able to undergo operation, but the surgeon must first satisfy himself that no internal strangulation is present, as such a lesion necessitates rapid pre-operative preparation with fluid and gastric lavage, followed by laparotomy. It is important to note that the conservative treatment of a mechanical obstruction may completely prevent the typical symptoms of pain and abdominal distension.

Strangulation-obstruction is associated with intestinal colic, vomiting and often considerable shock. Operation is imperative, and in the early case simple relief of the strangulation is sufficient. In the advanced case, the general condition of the patient is poor, and intestinal resection and anastomosis becomes a dangerous procedure. In such circumstances, immediate exteriorization of the gangrenous segment and resection is the best procedure. Catheters are secured in the bowel

ends, and the intestinal contents are collected and from time to time and are 'fed' into the distal bowel through the catheter. As soon as the patient's condition permits, usually about seven days later, a formal resection of the bowel ends is carried out, and the intestinal tract is reconstituted by a lateral anastomosis. This operation has proved to be a life-saving measure in a number of very grave cases of intestinal strangulation.

Treatment of Burns

By M. ROTHMAN, M.D.

J. TAMERIN, M.D.

and

J. G. M. BULLOWA, M.D.

(Abstracted from the *Journal of the American Medical Association*, Vol. CXX, 14th November, 1942, p. 803)

WHEN the surface of the body has been damaged by flame, scalds or chemicals, plasma escapes from the circulating blood into the injured tissue and from the surface deprived of protective coating. The resulting haemoconcentration, if uncorrected, may prove fatal. The exposed tissues provide an excellent culture medium without the usual dermal barrier to infection.

We have treated 32 patients suffering from burns which involved up to 45 per cent of body surface as measured by the scale devised by Berkow, with two deaths. These 2 patients died of secondary shock within the first forty hours. Sufficient plasma or blood was not available to counteract the haemoconcentration. One patient had the entire left upper extremity completely charred. The other had a third-degree flame burn involving 45 per cent of surface, mostly the trunk. There was no evidence of sulphadiazine toxic action on physical or laboratory examination during life.

The local treatment of these patients was application of 2.5 per cent sulphadiazine in 8 per cent triethanolamine solution in accordance with the method of Pickrell modified to provide rapid formation of an eschar by desiccation of the exuded serum. The method used was as follows:—

On admission of the patient to the accident ward, usual methods to combat shock are promptly instituted. These are frequent plasma infusions (as much as 2,500 c.cm.), adrenal cortex extract (1 c.cm. each day) and warmth. If the clothing is adherent, it is removed under morphine narcosis by soaking the patient or part involved in a tub of water at 100°F. Usually the clothing is not adherent and can be cut away. The patient is then placed on sterile sheets, and with aseptic technique the wound is cleansed. The surgeons wear caps, masks, sterile gowns and gloves during the procedure. Blisters are opened, and loose shreds of epithelium and skin are removed. The area is again sponged with sterile water at 100°F. If all the dirt is not removed by this technique we use the suds of white soap on cotton balls. Grease is removed with ether or benzine. The entire procedure is carried out without anaesthesia, rapidly and without pain. Green soap, gauze and scrubbing are not used.

The 2.5 per cent sulphadiazine in 8 per cent triethanolamine is sprayed on the surface of the wound every hour on the first day. After each application the surface of the wound is dried by fanning or, more recently, by an electric hair drier with warmed air. The same procedure is carried out every two hours on the second day, every three hours on the third day and every four hours on the fourth day. A heat cradle is used to maintain the body temperature at 90°F. Care should be taken to avoid any burns from this source. At all times aseptic technique is maintained. Physicians, nurses and visitors wear caps, masks and gowns.

A thin, pliable and translucent eschar forms in twenty-four to thirty-six hours and after the fourth day. Spraying is rarely necessary. No dressings are applied at any time. Sedatives are rarely required after the eschars are formed, and nursing care is minimal. Between the tenth and twelfth day the edges of the eschar tend to curl; at this time wet dressings of the

sulphadiazine triethanolamine solution are applied. As the eschar curls at its edges, a potential portal of entry for bacteria forms. Wet dressings of 2.5 per cent sulphadiazine in 8 per cent triethanolamine solution are applied at this stage in order to prevent secondary infection. Sometime between the twelfth and the twenty-second day the eschar will be completely separated, and its removal may be facilitated by cutting away the loose portions. When infection occurs, purulent material is readily visible because the eschar is translucent. A window is cut in the eschar to permit drainage. Wet dressings of the sulphadiazine solution are applied over the infected area until the infection has cleared. The procedure is the same for second and third degree burns. The spray has been used about the face, eyes and mucous membranes without injury. Similarly the 2.5 per cent sulphadiazine in 8 per cent triethanolamine solution is used on joints and fingers without constriction or limitation of motion. The eschar is pliable and does not crack.

Sulphadiazine blood levels, measurements of the urinary output and intake, and a study of the urinary sediment for red blood cells and sulphadiazine crystals were done frequently. None of the 32 cases studied exhibited any signs of sulphadiazine toxicity.

There were 7 white and 25 Negro patients. The ages ranged from 8 months to 57 years. Six were infants under 2 years of age, 7 were from 2 to 12 years of age and the remaining 19 patients were above 13 years of age. There were 10 burns produced by scalds of hot water, coffee or oil, and 22 by flame. Of the 24 admitted during the first twenty-four hours, 2 were infected. Of the 3 admitted in the second twenty-four hours, all were infected, and all 4 patients admitted between the second and fourth days were infected. Seven patients had received previous therapy with oils, ointments and grease. Secondary infection was present in 5 of this group treated previously with home remedies and in 4 of the 25 patients admitted without previous therapy. Of the 9 cases in which infection occurred, 6 entered the hospital after the first twenty-four hours. Of 1 patient with a beta *Streptococcus haemolyticus* infection of the wound where the eschar had peeled, the infection failed to respond to treatment with sulphanilamide powder, saline wet dressings and azochloramid but cleared promptly following the application of massive wet dressings of the sulphadiazine solution.

Cultures were taken from the wounds on admission, and the organisms usually found were *Staphylococcus albus* and *Escherichia coli*. Of the patients who had previous therapy or were admitted late, subsequent cultures showed beta *Streptococcus haemolyticus* in 3, alpha *Streptococcus* in 1 and *Staphylococcus aureus* in the remaining 4.

No patients are included in this analysis in whom less than 10 per cent of the skin area was involved. The area burned varied from 12 to 45 per cent of the body surface. The face was involved in 5, the extremities in 20, and the abdomen, back and chest in 20. All the patients had second and third degree burns. Eight of the 32 patients required skin grafting, usually in twenty-two to forty-four days after the accident. The skin of all the patients was supple.

SUMMARY

1. Treatment employing 2.5 per cent sulphadiazine in 8 per cent triethanolamine was found to be valuable in 30 of 32 patients with second and third degree burns, resulting in supple skin without toxic action from the sulphadiazine.

2. The prompt production of an eschar by spraying and drying alleviates pain and frequent dressings.

3. On the tenth day compresses of 2.5 sulphadiazine in 8 per cent triethanolamine may be used to prevent infection about the separating margin.

4. The solution may be employed without irritation or constriction about the face, mouth, eyes, joints and fingers.

Recent Trends in Gastro-Enterological Treatment

By ROBERT COOPE, B.Sc., M.D., F.R.C.P.

(Abstracted from the *Practitioner*, Vol. 149, November 1942, p. 277)

It cannot be said that there have been any recent epoch-making advances in gastro-enterological treatment. Sometimes, however, the best way of making progress is to go back a little in order to get on to the right road. The war has brought many changes in the way of living, and has also caused a shortage of supply of certain drugs. Both these apparent inconveniences may be useful if they purge gastro-intestinal therapeutics of the fussiness and faddiness which have been their particular bane. Even a shortage of newspaper may have compensations if it discourages the hitherto insistent invitations to self-diagnosis and treatment of indigestion or constipation.

DYSPEPSIA IN WAR TIME

In this country, as in others, the outstanding medical problem in the Forces has been that of dyspepsia. Payne and Newman's report in 1940 was followed by many other articles and communications, and a full discussion of the subject took place in March 1941 at the Royal Society of Medicine. It has become clear that no undue increase of the severer forms of dyspepsia has been determined by conditions in the Services; as Tidy summed it up:—

'What the present war has so far revealed is the unsuspected frequency of peptic ulcer and gastritis in the civilian population before the outbreak of war, and the not surprising fact that organic dyspepsia is incompatible with Army life.'

Moreover, many hospital physicians and surgeons in frequently bombed cities have noted that during the periods of heavy air raids, the incidence both of perforated ulcers and of hæmatemesis increased appreciably, although reliable statistics are hard to come by. War-time stresses, moreover, appear to be causing a considerable increase of relapses in civilian patients who are the subjects of gastric or duodenal ulcer.

PEPTIC ULCER

It is easy to see why individuals, whether in the Forces or not, can keep going in peace time, but break down in war. The peptic ulcer patient is usually a person of a particular 'personality trend', over-conscientious, sensitive, a worrier, apt to become depressed or to feel frustrated. If he can adapt his life to his ulcer, he may be able to do useful work, but he relapses under serious strains which he cannot meet. Untoward physical or mental strain upsets the equilibrium. Unaccustomed foods, hurried or irregular meals, excessive smoking, lack of fresh air from the black-out of bedrooms, lack of sleep, worries about family or finance or the distressful state of mankind, are all factors which may help to produce breakdown. Some or all of them are features of life either in the Services or in the changed conditions of the present industrial and civilian world.

The war has therefore emphasized the cardinal therapeutic principle that a carefully regulated mode of living is far more important than drugs for the patient with peptic ulcer. In the quieter conditions of peace it was found that, although the immediate results of hospital treatment were excellent, a follow-up over a period of ten years showed that only about one in seven remained completely free from symptoms, though about one in two were able to keep continuously at work, perhaps with occasional absence of a day or two. Tidy gives an illuminating example of the effect of regime:—

'A bus driver, the subject of peptic ulcer, once described his routine in civilian life. His trip took eighty minutes, and between each trip he had mild or light food, and frequently took Maclean's powder. His regime was thus not far different from Sippy's diet. With this routine he managed to carry on successfully

with occasional sick absences for a few days or a week or so. In the Army he was admitted to hospital after a few weeks.'

Treatment.—For the healing of an active ulcer, rest of body and mind is the most essential part of the treatment. Six weeks in bed is worth far more than any drug. Proper dieting is important, although there is no need to persist for too long in an over-rigid diet. A quiet life and a regime sensibly adapted to the disability are the best safeguards against relapse. As for drugs, belladonna is in short supply, and should be used only when there is clear evidence of troublesome pyloric spasm. Bismuth should not be used at all; it also is in short supply, is expensive, and is practically useless, both as an antacid or as a mechanical protector of the raw surface of the ulcer. Sodium bicarbonate has a low antacid value and produces a secondary rise of acidity; its use in the treatment of peptic ulcer should be abandoned. Magnesium hydroxide has disadvantages; it is laxative, and often produces rectal spasm or irritation. Magnesium trisilicate and aluminium hydroxide are the antacids of choice. There is a trend nowadays to administer vitamins also, especially vitamin C, more on the basis of medical common sense than of any specific effects obtained.

GASTRITIS

'Gastritis' and transient dyspepsias have also been common in the Forces; underlining again the extent of these disabilities in civilian life. The diagnosis of 'gastritis' is apt to be a cloak for ignorance, covering all sorts of dyspeptic upsets. True chronic gastritis can be revealed by the gastroscope, and is uncommon. In its simple catarrhal form it occurs particularly in persons with chronic nasal, buccal or respiratory disease; treatment of the primary lesion is essential, for, unless this is done, appropriate dieting (with the avoidance of irritating food) and lavage of the stomach with hydrogen peroxide, will give only temporary relief. Some dyspepsias which are labelled 'gastritis' are psychogenic, and usually respond to explanation and reassurance.

Transient dyspepsias are common. In civil life, the sufferer usually treats himself and recovers quickly; in the Forces, the change to a new type of life and an unaccustomed diet demand a period of acclimatization, and there is no call to treat the matter more seriously. Tidy points out that an analogous condition is the dyspepsia so often experienced at the outset of a holiday in a foreign country; it is cured by common sense, a temporarily lighter diet and a day or two of trisilicate or aluminium hydroxide therapy.

ULCERATIVE GINGIVO-STOMATITIS

Another condition made prominent by war conditions is ulcerative gingivo-stomatitis; many cases have already been noted both in civil and military life. Traumatic lesions of the gums, nutritional deficiency and local infection have all been claimed as factors, although opinion has not yet crystallized on the degree (if any) of their significance. Some patients have shown a vitamin-C deficiency, without obvious infection; in others, infection is present, the predominant organisms being anaerobic fuso-spirochaetes of the Vincent type. There is some evidence to suggest that on occasion the disease can be mildly epidemic; both contact infection and spread throughout a hospital ward have been described.

Treatment.—Until the cause is clearly established, it is wise to combine general and local treatment. Full doses of vitamin C, or alternatively nicotinic acid (150 mgm. daily for seven days, followed by a maintenance dose of 100 mgm. daily) are the drugs most in fashion at the moment. Local treatment consists of attention to any obvious chronic focus of disease (by tooth extraction, or even gingivectomy, if necessary) and by careful application to the lesions and to the inter-dental spaces either of 10 per cent chromic acid with hydrogen peroxide, or of gentian violet, followed by frequent peroxide mouth washes. This is done by means of small pledgets of cotton-wool soaked

in the solution; thoroughness and frequency of application are probably more important than the particular antiseptic which may be chosen. If there is a heavy infection by Vincent's organisms, local application of powdered novarsenobillon may be useful.

HÆMATEMESIS

A recent article by Bennett, Dow and Wright on severe hæmorrhage from the stomach and duodenum, led to a lively correspondence. Bennett and his co-workers have for some years made a careful study of patients suffering from this dangerous form of bleeding, using exact observations of blood volume to determine the amount of blood lost, and whether or not the bleeding had stopped. They emphasize the broad principles of treatment—rest for the body, the avoidance of dehydration, the need for sufficient non-irritating food to sustain the patient during a period of illness which may be prolonged, transfusion of blood when a further hæmorrhage may be fatal, and surgery (under conditions) in the few cases in which bleeding is unlikely to stop. They point out that associated pyloric stenosis may make the feeding even of fluids injudicious, by overloading the stomach and causing vomiting. They find no basis for the belief that recurrence of the bleeding is made more likely by blood transfusion, provided that it is given by drip at 30 to 40 drops per minute. An urgent need for blood may demand more rapid transfusion than this; the need must be determining factor, being more important than the possible consequence of recurrence of bleeding.

In the discussion which followed this paper, Sir Arthur Hurst brought an astringent common sense to the claim made by other correspondents for the routine use of the Meulengracht type of diet, emphasizing that lack of fluid rather than lack of food is the immediate danger. My colleague, Mr. H. C. W. Nuttall, intervened to urge the need for early surgery if the bleeding is due to erosion of a fair-sized artery.

Treatment.—The crux of the matter is surely this. Most cases of hæmatemesis are due to bleeding from a peptic ulcer, and will recover with proper medical treatment. Mild cases will not be harmed by the liberal Meulengracht diet, and more severe ones will usually survive it; though it involves a needless risk, seeing that if patients are treated adequately by rest, including the administration of morphine, and the avoidance of dehydration, helped by blood transfusion when necessary, none should be lost in the first few days by reason of lack of food. The serious problem is the comparatively rare patient whose bleeding is due to erosion of an artery. Meulengracht himself seems to be content to allow for a basic death rate of 1 to 2 per cent, presumably due to the arterial hæmorrhage which will not stop of its own accord—a judgment which seems rather hard on patients with this catastrophe, few though they be. Unfortunately the discussion of gastric or duodenal hæmorrhage has been too much concerned with estimating the mortality as a percentage of all cases, mild, moderate and severe, and too little with the occasional patient in direct jeopardy of his life. In practice, the problem is personal and not statistical. The practitioner is faced with a bleeding patient, who *may* be one of the small percentage with erosion of a fair-sized artery. If this is so, must he throw in his hand because of the 'certain basic death rate'? Here medical treatment means death; will surgery kill the patient too?

The pros and cons of *surgical intervention* are worth recapitulation. On the one hand, it is argued, it is difficult to be sure that a particular, profuse hæmorrhage is 'due to erosion of a fair-sized artery; even with full facilities for estimations of blood volume, it may be some days before the practitioner knows whether bleeding is continuing or not. Thus, if early operation is done, it may be found to have been unnecessary. In the hands of all but the most skilled abdominal surgeons the patient will probably not survive what is in any case a grave major operation. Even in skilled and experienced hands, it may be impossible to stop the bleeding because of the friability

of the surrounding ulcerated tissues. Finally, there is always a slender chance that a small artery may become sealed by clot.

On the other hand, it is generally agreed that really severe hæmorrhage is a surgical emergency, even though a high mortality is associated with operation. In older people with inelastic arteries, erosion of an artery is almost invariably fatal. The prognosis depends not only on the amount of blood lost, but on the rapidity of its loss; it is therefore disastrous to wait until one is absolutely sure that a massive bleeding will not stop of its own accord. Time is wasted, also, because it is not always appreciated that the bleeding may temporarily cease because of the fall of blood pressure directly due to the loss of blood; with a rise of blood pressure following transfusion and anti-shock treatment, the bleeding begins afresh. It is not, as is sometimes thought, that an effectively occluding clot has been disturbed by the transfusion of blood. Again, until the surgeon has opened the abdomen of the urgent 'emergency', no one can know whether the lesion is accessible to surgery or not; in any case, the gloomy outlook of certain physicians on this point is not supported by the experience of such skilled abdominal surgeons as Finsterer, Borer, Gordon-Taylor, Nuttall and others. Finally the surgeons complain that usually the request for their help is delayed until it is too late, so that operation is hopeless because of tissue anoxia, dehydration, and a nephrotic syndrome with retention of nitrogen and with oedema caused by renal failure due to low blood pressure and anæmia, and that the friability of tissues is largely due to these very changes; and they point out that more than half the patients treated medically die if the hæmorrhage recurs.

Summing up, in the great majority of patients suffering from hæmatemesis, surgical intervention is unnecessary, and may be harmful; with rest, morphine, good nursing and the prevention of dehydration, helped if need be by blood transfusion, the outlook is usually excellent. A few patients, however, have an eroded artery; sealing of it by clot is extremely unlikely, and the bleeding continues until it kills the patient. Here, early surgery is the only hope of saving life. How then is the physician to decide whether or not a patient needs this early surgical intervention? Bennett and his colleagues rightly speak of the 'terrible dilemma' when the slender chance of the bleeding stopping of itself has to be weighed against the equally slender chance of the patient surviving a major operation. Much of the 'terribleness' of the dilemma is due to the lack of unequivocal clinical indications for early operation.

In making his decision, the practitioner may recall that, nine times out of ten, severe hæmatemesis is due to peptic ulcer; the remainder are most frequently associated with portal cirrhosis, splenic anæmia or splenomegalic leukaemia. In this latter group, either there is no history suggestive of ulcer, or the spleen is enlarged; although sometimes, after profuse bleeding, the spleen may shrink so considerably that it cannot be felt. The older the patient and his arteries, the less likely is bleeding from even a small eroded artery to stop, and the more dangerous it is to the general tissue nutrition. Immediate hæmoglobin readings are of no help, for it is some hours before the fluid portion of the blood is restored by means of absorption from the tissues; therefore until this happens the hæmoglobin percentage is not lowered. Even the clinical signs of severe blood loss—pallor, restlessness, air hunger, low blood pressure and rising pulse rate—are not necessarily cardinal indications for operation, because adequate transfusion of blood may resuscitate the patient and the bleeding may still cease of its own accord, particularly if the patient is young.

My own view is that, as a rule, the physician can afford to delay for a short time after an initial profuse hæmatemesis, to see the effect of adequate blood transfusion. If the patient has an eroded, patent artery, the restoration of blood pressure will cause spurting of blood again, so that before long the stomach is filled sufficiently to cause a further considerable

vomiting of blood. Thus, within a few hours it becomes reasonably clear whether or not the bleeding persists. With continuing profuse hæmorrhage, only operation gives the patient a fighting chance for life.

Sometimes the picture of *secondary hæmorrhage* is seen with its interval of 'silent necrosis'. At first, the bleeding comes from a smaller arterial branch; the bleeding stops and the patient is restored by blood transfusion. A few days later, however, a massive hæmorrhage announces erosion of the main artery. Here, again, immediate surgical intervention is indicated. The surgeon must be experienced enough to be content to do the minimum necessary for the arrest of the bleeding, and to do it quickly; blood which has been lost is replaced by continued transfusion. It is true that owing to the rich plexus of blood vessels in the duodenum, or to the pathological condition of the ulcer itself, some form of resection is sometimes the only means of stopping the hæmorrhage; it must involve the simplest procedure possible, for this is no occasion for any 'long term policy' operation, such as gastrectomy directed to preventing further ulceration. On this point, Nuttall's views are helpful.

CONSTIPATION

It is to be hoped that war conditions will have a salutary effect on the widespread excessive use of aperients. Liquid paraffin and phenolphthalein are two of the drugs which are in short supply; many people are already finding compensation in the natural laxative effect of the present wheatmeal bread. Many patients use aperients as a substitute for sound living—plenty of work and exercise, plenty of simple healthy food (the *bulk* being most important), and fluid (two extra glasses of water a day will often make a surprising difference to 'the bowels').

ULCERATIVE COLITIS

The value of sulphaguanidine in the treatment of bacillary dysentery has led to its trial in ulcerative colitis. As yet, the results are uncertain; there have been both successes and failures. Extended therapeutic tests should before long allow an assessment. A more recent intestinal antiseptic with high antibacterial powers, low toxicity and poor absorbability, is succinyl sulphathiazole, and no doubt this will also be tried. Another possible form of treatment for this dread disease is likely to be explored, i.e., colonic lavage, through the old-fashioned appendicostomy opening, by solutions of sulphonamide derivatives. Terminal ileostomy, earlier reports of which promised great things, has not given consistently successful results. Meanwhile, the basis of treatment remains—the building up of the patient's general and local condition by good, residue-free food, iron, blood transfusions, belladonna for painful spasm of the colon, and kaolin or aluminium hydroxide by mouth. Many physicians, of whom I am one, have come to discard routine lavage of the colon, even though it is done with exceeding care; most patients find it painful and exhausting, and dread it.

FLATULENCE

The general practitioner is particularly concerned with the treatment of flatulence, because it is always such a common complaint; in war time it appears to be even commoner than in times of peace. War diet, and especially bread, are often blamed for it; but it must be remembered that fermentation or putrefaction of poorly digested food is the least common cause of it. Air swallowing, conscious or unconscious, is by far the most frequent factor, and in the absence of such disorders as congestive heart failure, gall-bladder disease or some other obvious lesion of the gastrointestinal tract, the determining cause will usually be found to be either neurosis or chronic constipation. Chronic fatigue due to the stresses of war often produces an appreciable amount of flatulence with which many patients put up philosophically; others are worried and seek advice. Symptomatic treatment may provide relief, but it is the patient who needs to be treated, as well as the symptom; a difficult problem

in war time, when he or she is so often too busy or too important to 'let up' and take a rest. Under such conditions the practitioner must try to help his patient to some form of working compromise. Prostigmin bromide in 15 mgm. tablets, four times daily, has recently been reported as giving excellent results in symptomatic relief; it acts by increasing the tonicity of the intestine.

DISORDERS OF THE LIVER AND BILE PASSAGES

There is little to add to Newman's review of 'Cholagogues and Drugs acting on the Liver' which appeared in *The Practitioner* of November 1940. In America, a good deal of experimental work is being done on the effect of different dietetic factors on the liver cell, and some interesting clinical applications are foreshadowed. The protective action of glucose is well established; an adequate protein supply in the diet is of equal importance in increasing the resistance of the hepatic cell to injury by toxic agents. Again, excessive fat in the liver over a prolonged period is found to contribute to the development of cirrhosis; it is suggested that alcoholic cirrhosis is due not only to toxic damage of the liver cell by alcohol, but also to the chronic fatty infiltration which is a feature of it. Animal experiments show that the same mechanism is involved in malnutrition, deficient diet and especially vitamin-B deficiency. As yet, the significance of these experimental findings for practical clinical work is not clear, unless it is to emphasize the simple fact that a patient cannot expect a healthy liver cell if he is not living a healthy life—a lesson which the patient often finds the most difficult of all to accept from his medical adviser.

Treatment.—Reflex spasm of the musculature of the extra-hepatic biliary tract from cholecystitis or gall-stones often prevents proper emptying of the gall-bladder; relaxation is best obtained by belladonna. Egg yolk and cream mixture is also effective, much more so than olive oil; it causes a slight initial contraction, followed two to three hours later by relaxation. A paper from L. S. P. Davidson's department in Edinburgh throws serious doubt on the significance and therapeutic value of biliary drainage through the duodenal tube; the inflammatory material 'drained' from the biliary passages is, it appears, produced by the technique itself. The use of salicylic acid as a biliary antiseptic in cholecystitis is now giving place to the more effective administration of sulphonamides.

Trichlorethylene as a General Analgesic and Anæsthetic

By C. LANGTON HEWER, M.B., B.S., D.A.

(From the *Proceedings of the Royal Society of Medicine*, Vol. XXXV, May 1942, p. 463)

ABOUT two years ago, I was asked by Dr. Charles Hadfield, secretary to the combined Anæsthetics Committee of this Section and of the Medical Research Council, to investigate the possibilities of trichlorethylene as a general anæsthetic.

In June 1941 I made an interim report in the form of a short article in the *British Medical Journal*. The results obtained were so encouraging in certain directions that since that date I have continued to use the drug, and I now hope to put before you the conclusions I have reached.

Physical properties.—Trichlorethylene was first described in 1864; its chemical formula is $\text{CCl}_2:\text{CHCl}$. It is a heavy colourless liquid with a specific gravity of 1.47 at 15°C. and a boiling point of 87°C. The odour resembles that of chloroform without its pungency. In view of the similarity of the two fluids in respect of both weight and smell, I have suggested to the manufacturers that trichlorethylene prepared for anæsthesia should be coloured either blue or green. This would readily distinguish it from chloroform which is either colourless or tinted red by one maker.

Trichlorethylene is not inflammable in any circumstances nor will its vapour explode when mixed in any proportion with air, oxygen or nitrous oxide.

The pure drug tends to decompose in strong sunlight with acid formation, and should therefore be stored in stoppered amber bottles. The addition of 0.01 per cent thymol retards decomposition, and this has been done in the case of the product known as 'trilene'. As an extra precaution, the manufacturers suggest that it should not be used for inhalation purposes after twelve months from the date of bottling.

The cost of purified trichlorethylene is very reasonable as if supplied in lots of 8 lb. to hospitals the price is 3s. 6d. per lb. It has been estimated that the average cost per administration works out at about 4d.

Commercial uses.—Trichlorethylene is chiefly used for the dry-cleaning of clothes, the de-greasing of metals and the de-waxing of lubricating oils. For these purposes, the fluid is sold under a variety of trade names such as chlorylene, gemalgene, trethylene and triklong. These preparations may contain a variety of impurities and should not be used as anæsthetics.

It is of some interest to know that addiction to trichlorethylene is not very uncommon amongst industrial workers. The vapour used for de-greasing metals rises in a vat and is condensed by cold pipes. Some workmen find considerable pleasure in leaning over the sides of the vats and inhaling the vapour until they feel intoxicated.

Industrial poisoning.—On the Continent several writers have recorded cases of industrial poisoning in factory workers when crude trichlorethylene was used. Symptoms such as giddiness, vomiting, optic neuritis and various palsies have been described (Plessner; Gerbis). Some cases have proved fatal (Stüber). It should be noted that all the patients had been exposed to the vapour of commercial trichlorethylene which, as already mentioned, may contain a great variety of impurities. Workers constantly exposed to trichlorethylene vapour in aeroplane works are said to be liable to dermatitis (Schwartz and Russell).

External application.—A few years ago, the use of trichlorethylene was recommended as a skin purifier and to clean up burns and dirty wounds (Trumper and others). For these purposes Imperial Chemical Industries Ltd. produced a specially purified and stabilized liquid under the name 'trilene'. With the exception of some pure trichlorethylene made and generously supplied by Mr. C. Chalmers who originally suggested the investigation, all cases have had trilene for inhalation.

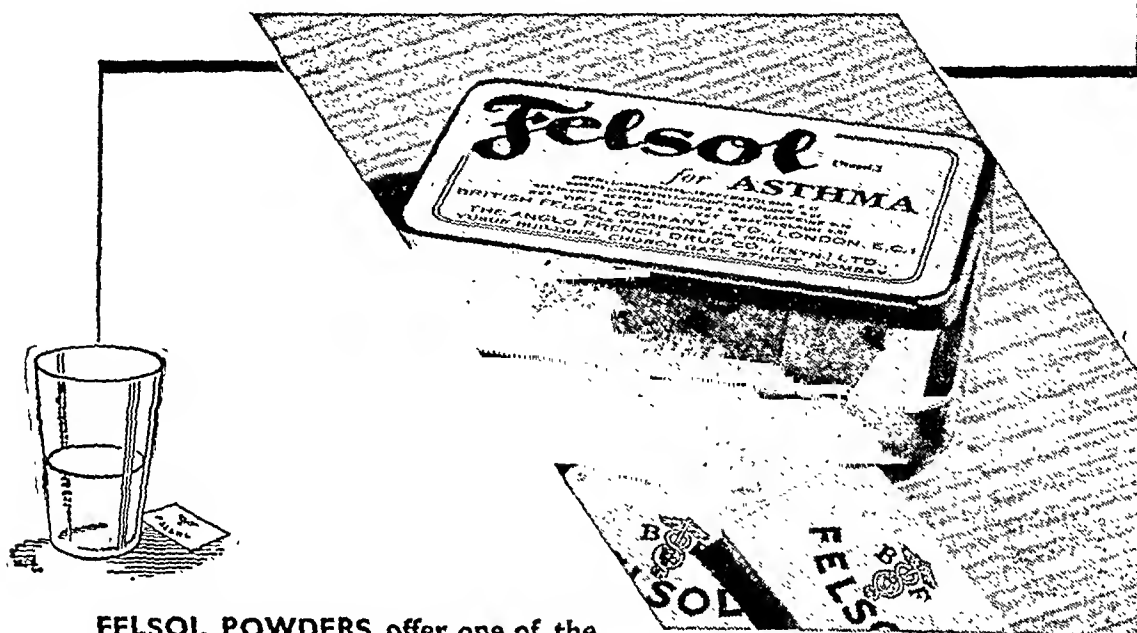
Therapeutic inhalation.—The drug has been used for some time to relieve the pain of trigeminal neuralgia. For this purpose, the vapour is inhaled from broken capsules as in the case of amyl nitrite. The origin of this procedure is worth noting. Two separate observers reported that patients suffering from chronic trichlorethylene poisoning showed complete bilateral paralysis of all divisions of the trigeminal nerve (Plessner; Gerbis). It was supposed that the drug had a specific action on this nerve and its administration for the relief of trigeminal neuralgia was suggested (Oljenick), and shown to be effective (Glaser). It appears to me quite certain that the relief from pain is not due to any effect on the trigeminal nerve but to the state of general analgesia which is induced and to which I will refer later. This seems to be an example of faulty reasoning leading to the desired result.

Experimental work on animals.—During the past twenty-one years several workers have fully investigated the effects of trichlorethylene on animals.

Joachimoglu found that the pure vapour was not irritating to the respiratory tract and that inhalation was not followed by hæmolysis or by fatty degeneration of the liver.

Herzberg reported that specimens of spleen, liver, kidney, pancreas, adrenal, diaphragm, heart, lung and pectoral muscle taken from three dogs killed by overdose of trichlorethylene after having been deeply anæsthetized for periods of two and a half to three and a half hours showed no gross or microscopic pathological changes.

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Krantz and others anesthetized the same rats repeatedly (up to 30 times) with trichlorethylene. The animals were then killed and the various organs examined. Although some pathological changes were found, they were in the main slight and inconclusive. In rabbits slight hyperglycemia was noted. The same workers found that anesthesia could not be obtained by the rectal administration of the drug and that nerve conduction was not affected by the local application of trichlorethylene.

Lande and others anesthetized guinea-pigs, rats and mice with trichlorethylene daily for two and a half months, the duration of narcosis being from fifteen minutes to one and a quarter hours per day. After death it was hardly surprising that some inflammatory changes in the liver and kidneys were noted.

From these extremely severe tests it may reasonably be concluded that in the usual experimental animals, trichlorethylene is only slightly toxic—certainly much less so than chloroform.

Previous work in human anaesthesia.—The only published work which can be traced is that on a series of 300 patients anesthetized with trichlorethylene by Striker and others in America in 1935. These were all short administrations for minor operations, and in some instances analgesia only was produced. Eight of these patients became violent in the second stage, and the third stage of anaesthesia could not be reached. One patient stopped breathing from an overdose but recovered after artificial respiration. After-effects were slight, and on the whole the drug was regarded as a satisfactory anaesthetic.

In the following year the Council of Pharmacy and Chemistry of the American Medical Association considered the evidence for the usefulness of trichlorethylene and concluded that 'the case had not been completely made out.'

Details of present investigation.—The observations which follow are based upon about 400 administrations. Most of the commoner major and minor operations were performed under trichlorethylene anaesthesia, or analgesia, their duration varying from five minutes to five hours and forty minutes; the latter operation being the removal of a cerebral tumour from a woman with bronchiectasis. The administration in this case was by my colleague Dr. B. Rait-Smith and I am glad to say that the patient survived. The patients' ages were between 14 months and 81 years and included Service casualties, air-raid casualties and ordinary hospital civilian patients.

Methods of administration

It at once became evident that an open mask administration was impracticable owing to the low volatility of trichlorethylene. In America a special apparatus has been devised to vaporize the drug incorporating an air compressor driven by an electro-motor (Jackson). As we had neither the wish nor the facilities to develop complicated machinery, we began by putting trichlorethylene in the chloroform bottle of a continuous-flow apparatus and using it as an adjuvant to nitrous oxide and oxygen. When used with partial rebreathing this method was quite satisfactory. In most cases a face-piece was employed, but, when indicated, a nasal or oral endotracheal tube was passed. Muscular relaxation was usually ample for intubation to be performed without difficulty.

If the CO₂ absorption technique is used, it is essential to have the vaporizer in the patient's respiratory circuit. Insufficient concentration of trichlorethylene is obtained if the basal oxygen feed alone is used to vaporize the drug as in the single-phase Waters' system or in the standard two-phase apparatus as supplied to the E.M.S.

After a fairly full investigation of trichlorethylene as an adjuvant to nitrous oxide and oxygen, it was decided to find out whether the drug had any possibilities when given alone. After various trials and errors, a simple draw-over apparatus was adapted from a Walton ether bottle. In order to produce analgesia, only a small bottle without a rebreathing bag is sufficient, but to ensure that the third stage of anaesthesia is reached, a large bottle containing a wick is necessary and some

rebreathing is desirable. By plugging in a similar ether bottle in series, a compact apparatus results which is adaptable to practically any type of inhalation analgesia or anaesthesia including endotracheal work. In the latter case it is, of course, essential to have an air-tight fit, either by plugging or by the use of a ballooned tube. Dr. H. R. Marrett, Senior Resident Anaesthetist at Hill End Emergency Hospital is largely responsible for the design of this apparatus which (with one bottle) can be produced to sell retail at about £5 10s.

When used continuously for general anaesthesia, about 13 c.c. of trichlorethylene per hour are consumed.

Stages and signs of analgesia and anaesthesia

In most respects trichlorethylene resembles chloroform rather than ether.

During the first stage, some degree of *general analgesia* always seems to be present. This comes on after a few breaths and varies in degree from some numbness to pain in resistant patients to that of absolute analgesia during which can be carried out such procedures as wedging plasters, insertion of bone pins, cystoscopies, painful dressings, etc. The sensation of general analgesia is one of curious detachment. One patient rather aptly described it by saying that he appeared to be watching himself being operated upon as if he was a disinterested third party. Two patients suffering from trigeminal neuralgia were given trichlorethylene and the pain was practically abolished in both cases, but at the same time sensitivity to pain was greatly diminished in all areas. I am convinced that the relief in this condition is due to general analgesia and not to any specific effect upon the trigeminal nerve, in spite of the statement made in the book just published by no less a pharmacological authority than Adriani. Trichlorethylene exerts the most potent and rapid analgesia of all the volatile drugs with which I am familiar, including nitrous oxide, and it appears to me that it might be of very great use, especially under war conditions where the absence of heavy and complicated apparatus, and hot water jackets, gas cylinders and inflammable vapours are all desirable.

The second stage of anaesthesia is not usually marked but occasionally violent excitement occurs.

The third stage is characterized by quiet automatic respiration and a pupil which is usually small. The eye reflexes are similar to those obtaining with chloroform.

Effects on respiratory system

The odour of trichlorethylene is not pungent nor does its vapour appear to have any irritant effect upon the respiratory passages. It follows that the vapour concentration can be increased rapidly leading to a short induction of anaesthesia. No excessive salivation or secretion of mucus was noticed even if premedication had been inadequate or badly timed. Several major thoracotomies were done under trichlorethylene anaesthesia as were many other operations upon patients suffering from bronchitis, bronchiectasis and active phthisis. In no case could any exacerbation of the pulmonary disease be attributed to the anaesthetic. The depth of respiration was not appreciably altered but in about 30 per cent of patients receiving the drug as an adjuvant to nitrous oxide and oxygen, some increase in the rate concerned. This usually subsided after fifteen to twenty minutes but in a few cases it persisted. When present, this rapid breathing is a definite disadvantage in thoracic surgery. The tendency was not so marked when trichlorethylene air was used. On one occasion an overdose was inadvertently given. Respiratory arrest occurred, but no difficulty was encountered in restoring natural breathing. The pulse remained steady throughout.

Effects on cardiovascular system

The blood pressures usually remained within normal limits except for some rise when the second stage of anaesthesia was marked by much excitement. Dilatation of the vessels in the skin and subcutaneous tissues such as occurs with ether and cyclopropane was not

seen, and surgeons frequently commented upon the absence of capillary oozing. This was particularly noticeable in nasal and in ophthalmic surgery. The pulse rate was generally raised slightly as in the case of most inhalation anaesthetics.

Particular attention was paid to the cardiac rhythm as trichlorethylene contains three chlorine atoms in its molecule, and at least two other compounds with this characteristic (chloroform and trichlorethanol) can cause grave cardiac irregularities and even primary cardiac failure (Wood; Hewer and Belfrage). Clinically few cardiac irregularities could be detected apart from sinus arrhythmia in young patients which disappeared when full anaesthesia was reached. An irregular pulse was definitely less common than with cyclopropane, and several patients with extrasystoles before operation showed a regular rhythm after anaesthesia had been induced with trichlorethylene. This is, of course, common with inhalation anaesthesia generally. Two cases of partial thyroidectomy had auricular fibrillation which remained unchanged throughout the anaesthesia.

The possibility of primary cardiac failure still cannot be entirely excluded, but so far I have not heard of such an event although a large number of administrations have now been made. Since the publication of my original paper, 48 hospitals have been using trichlorethylene and it has been estimated that at least 10,000 patients have been anaesthetized with it.

Dr. K. D. Keele kindly arranged for electrocardiograms to be taken during the induction of anaesthesia in 33 cases. A Cossor-Robertson cardiograph and later a Cambridge instrument were installed in one of the anaesthetic rooms, and direct visual observations as well as photographic records were made before and during induction. In most of the cases so observed there was no alteration in the tracing apart from a slight decrease in the sinus tachycardia as the third stage of anaesthesia was reached. In one instance regular auricular extrasystoles alternating with normal systoles occurred over a period of some three minutes and then ceased. In two other cases occasional ventricular systoles were seen during the second stage, but disappeared as the third stage was reached. In no case were multiple ventricular extrasystoles seen. These were particularly looked for in view of their comparatively frequent occurrence during chloroform anaesthesia. This limited number of observations suggests that there is no evidence of any particular cardiac danger with trichlorethylene.

Muscular relaxation.—The degree of muscular relaxation obtainable with trichlorethylene is variable. As a general rule, operations upon the head, neck, thorax and limbs present no difficulty, but adequate relaxation for major abdominal surgery is not always readily available. It is possible that a really deep plane of narcosis may produce the desired result, but I have always played for safety and changed over to ether in preference to pushing trichlorethylene. One opportunity occurred for observing the effect of the drug upon the uterine musculature. An abdominal hysterectomy was performed to terminate pregnancy on account of active phthisis. The surgeon remarked upon the exceptionally good retraction of the uterus following extraction of the foetus. After an average of twenty minutes' administration, it was found that the vapour concentration of trichlorethylene could be greatly reduced without prejudice to muscular relaxation.

Effects on sugar metabolism.—Dr. A. Jordan kindly made blood-sugar estimations before, during and after anaesthesia with trichlorethylene. In no case was there much disturbance, and taking an average, it could be said that there was no significant change. This contrasts with the rise constantly seen with chloroform and ether (Hewer).

One diabetic patient was included in the series. An abdominal operation lasting one hour fifteen minutes was performed under nitrous oxide-oxygen-trichlorethylene anaesthesia. The sugar tolerance was tested one week after operation and was found to be unchanged.

Effects on blood urea.—Blood-urea estimations were made by Dr. Jordan before, during and after anaesthesia. The changes were so slight as to be within the range of experimental error. Here again the contrast with chloroform and ether is marked.

After-effects

If analgesia only has been produced, it is unusual for any after-effects to occur. Occasionally slight dizziness or headache may be present for a short time.

Of the first 127 patients anaesthetized for a great variety of operations, 61 per cent had no nausea or vomiting, 26 per cent had nausea or slight vomiting and 13 per cent moderate or severe vomiting; 5 per cent complained of headache. Those who had had previous experiences with ether nearly always commented favourably upon the absence of an unpleasant taste and smell.

In most cases the urine was tested as a routine on the day after operation. In one instance only was the presence of albumin found and acetone was always absent. This is in marked contrast with other anaesthetics. For example albuminuria has been found almost constantly after the prolonged administration of ether and in about 20 per cent of patients anaesthetized with chloroform (Stephen). Again, acetoneuria has been demonstrated in 67 per cent of patients operated upon under all forms of general anaesthesia and in 85 per cent under local analgesia (Schulze). No pulmonary complications were observed, and, as already mentioned, existing lesions did not appear to be affected.

Summary and conclusions

So far as our present knowledge goes, trichlorethylene when inhaled resembles chloroform in its effects but is less potent as an anaesthetic, more potent as an analgesic and less toxic.

The advantages of the drug are:—(1) The absence of irritation to the respiratory passages; (2) the comparative absence of superficial oozing from cut tissues in patients under its influence; (3) the high degree of analgesia available; (4) the non-inflammability of its vapour; (5) its relative cheapness and availability and the fact that no complicated apparatus is necessary.

The disadvantages are: (1) Complete muscular relaxation is sometimes difficult to achieve; (2) the respiratory rate is sometimes raised.

Tourniquet for Heart Failure

(From the *British Medical Journal*, Vol. II, 12th December, 1942, p. 702)

THE application of venous tourniquets to the limbs has been practised instead of venesection in cases of heart failure for a number of years since its introduction by Danzer in 1928. The peripheral venous bed is turned into a reservoir in which may be stored about 12 to 15 per cent of the circulating blood volume. The method was shown to be effective in the treatment of left ventricular failure by Weiss and Robb in 1933. An interesting light is thrown on its mechanism by Kountz, Smith, and Wright, who used a machine which maintained inflation of cuffs placed on all four limbs for four minutes and deflation for one minute, the latter so arranged as to operate on each limb in turn, so that three limbs were always congested. The authors found that cases of left ventricular failure responded very well, but that those with right ventricular failure, as in acute or chronic cor pulmonale, did not. The point of interest was this: while the venous pressure fell and kymographic pulsation of the heart diminished (the expected results of lessening the venous return), the size of the heart, as measured by its transverse diameter, increased appreciably in normal subjects and in two patients with mitral stenosis. Cases of left ventricular failure showed no such increase. On the contrary, two of them showed a smaller heart shadow during venous compression. No explanation of this phenomenon is available. Cardiac output was not

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The 'Elastoplast' bandage was removed, and the patient given exercises to restore full power to the quadriceps.

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☆ The details given are of an actual case. The illustrations are made from photographs taken of this case.

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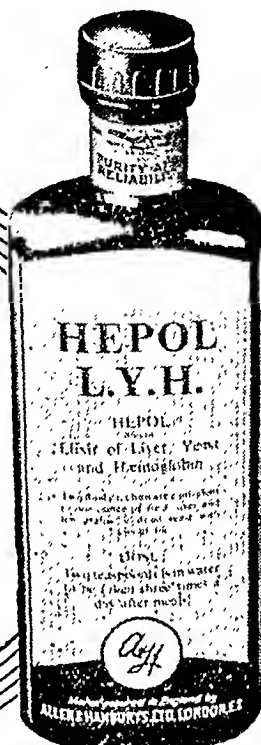
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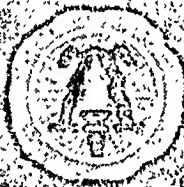
Hæmoglobin, being an organic compound of iron, does not produce the gastro-intestinal symptoms that are sometimes produced by inorganic preparations of iron. Animal or vegetable sources of iron are recognized as desirable constituents of the diet in simple anæmias.

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measured; but as neither the pulse rate nor the blood pressure altered appreciably, whereas the venous pressure and amplitude of cardiac pulsation fell, it may be assumed that the cardiac output fell too. Before looking for the solution the facts should be confirmed, for very few cases seem to have been studied in this paper. However, the method of treating orthopnoea and paroxysmal cardiac dyspnoea by compression of the limb veins is again brought before the notice of physicians.

Reviews

GLEANINGS FROM MY RESEARCHES. VOLUME II:—MALARIA, HÆMOLYSIS AND OTHER SUBJECTS.—By Sir Upendra Nath Brahmachari, Kt., M.A., M.D., Ph.D., F.R.A.S.M., F.N.I. 1941. Published by the University of Calcutta. Pp. xviii plus from 463 to 808. Illustrated

In January 1900, a young house-physician of the Medical College Hospitals, Calcutta, published in the *Indian Medical Gazette* a short paper on septic endocarditis. This may have been his first publication. That young house-physician is now Sir Upendra Nath Brahmachari, the author of this book.

Sir Upendra Nath is best known for his work on chemotherapy of kala-azar. He was the pioneer of chemotherapy in India, and his reprinted papers on this subject, and on kala-azar in general, formed the bulk of volume I of the present publication. This first volume was reviewed by Dr. L. E. Napier in our October 1941 number, and it is quite unnecessary for the present reviewer to add anything to the tribute paid in that review to the work of Sir Upendra Nath.

The second volume of these 'gleanings' was apparently published in 1941, but has only just reached us. It consists of the reprints of 64 papers published between 1900 and 1941. These papers have been published in about eighteen different journals, mainly Indian journals, but English and American journals are included. The main subject of the present paper has been classified by the reviewer as follows—quinine hæmoglobinuria, blackwater-fever, hæmolytic, etc.—19 papers; the chemistry of quinolin compounds and the chemotherapy of malaria—11 papers, the chemotherapy of syphilis and kala-azar—several papers; other subjects include Burdwan fever, quartan malaria, quinine therapy, diagnosis of malaria, cholera, blood-sugar in Indians, endocarditis, athetosis, hysteria, acute yellow atrophy, angio-neurotic oedema, hæmophilia, five-day fever, cirrhosis of the liver, influenza, filariasis, and meningitis. It will thus be seen how wide was the sphere of the author's interest and activity, particularly in his younger days before he became famous for his work in chemotherapy.

With such a large number of papers on such a great variety of subjects, it is naturally very difficult to give any detailed review. All the papers are of interest; in some the interest is mainly historical; some show the young physician grappling with problems which have now been partly solved. Many problems discussed here are, however, still unsolved, such as the mechanism of hæmolytic in blackwater fever, the relation of the administration of quinine to this phenomenon and other allied matters, which for many years formed one of the main subjects of the author's study. These papers may still be read with interest.

The work of Sir Upendra Nath, like that of most other pioneers in medicine, has given rise to controversy. One article reprinted in this volume is devoted to a very interesting summary of the history of the treatment of kala-azar with urea-stibamine; in this article Sir Upendra Nath gives details of the work which led to the preparation by him in 1920 of urea-stibamine, and to the wide adoption of this remedy for the treatment of kala-azar. This article and other shorter publications reprinted in this volume were written largely

with the object of correcting certain published statements made by a British writer famous for his work in tropical medicine. There is no doubt that the production in India of urea-stibamine by Sir Upendra Nath saved a vast number of lives that would otherwise have been lost, and greatly facilitated the control of kala-azar in India.

In a recent editorial in this journal, it was pointed out that for general treatment of kala-azar, the pentavalent compounds still hold a pre-eminent place, and, of these, urea-stibamine is probably as good as any.

J. L.

MEDICAL JURISPRUDENCE AND TOXICOLOGY.—

By John Glalster, M.D., D.Sc. Seventh Edition. 1942. E. and S. Livingstone, Edinburgh. Pp. viii plus 671, with 132 illustrations, several in colour. Price, 28s.; postage, 9d.

This book has been completely re-written; this task would not have been an easy one even in peace-time. The size of the book has been reduced by 76 pages, and this has been made possible by omitting certain matter which is considered to be outside the scope of both the student and the practitioner for whom the book is primarily intended. In spite of this, the new edition has lost none of its original character.

The balance between the Medical Jurisprudence and Toxicology is well maintained. References have been very neatly relegated to the end of each section. The index is easily consulted, and a reference to any poison can be made quickly.

The illustrations given in this new edition are a great improvement on those of the former editions; some of the old ones retained are much clearer, while the new ones are excellent; the colour plate, figure 46, showing the effects of burning caused by accidental ignition of a motor car is very good.

The pages dealing with the examination and identification of hairs and fibres show that the author has made a very deep study of this subject. There is much information here that is not available in most textbooks.

The author was formerly Professor of Forensic Medicine at the University of Egypt, Cairo, and Medico-Legal Consultant to the Egyptian Government where many of the medico-legal problems are similar to those in India. We would have welcomed a little more reference to some of these problems. A short appendix dealing with post-mortem changes, as well as a short description of poisons peculiar to the East, would be useful.

One last suggestion may be ventured. A description of the microscopic appearances of certain leaves, roots, seeds, such as datura, aconite, cannabis indica, nuxvomica, would have been welcome. The microscope is now as much a part of the equipment of the student and practitioner as is the stethoscope, and examinations of stomach contents are not only a very fascinating study but are of very real value in cases of poisoning.

The price of the book has been unavoidably increased from 25 shillings to 28 shillings, but when compared with American productions, the book is still moderately priced.

The book is recommended with confidence, and the publishers are to be congratulated on a very beautiful production, handicapped as they were by war-time restrictions.

D. R. T.

MEDICAL RELIEF IN EUROPE: QUESTIONS FOR IMMEDIATE STUDY.—By Melville D. Maackenzie, M.D. 1942. Oxford University Press, London. Pp. 67. Price, 2s. Obtainable from Oxford University Press, Bombay and Calcutta

The impression that one gets from reading this little pamphlet is that it is written to order. There is a lack of spontaneity. The problems are stated rather than solved, and while we have no doubt that most of these problems will certainly arise, there will probably be others that will overshadow them.

The two diseases with which the writer deals mainly are typhus and malaria; he is probably right to pick out

these two diseases, but he is judging on past experience, and history has not repeated itself in this war in quite the way we have expected. It is a pity, especially when a book is written mainly for the laity, that it should contain statements that many will know are not true. The statement 'No vaccine exists that is known to give protection to human beings' is untrue, though it would have been correct to say that up to the present it has not been possible to produce a really satisfactory vaccine for use on a large scale. A few lines lower the author writes 'Twelve to fifteen days elapse after the individual is bitten before he develops the disease'. It is very much more than a matter of academic importance that the disease is not transmitted by the bite, but from the crushed louse or, most important of all, from the dried faeces of lice, which may blow about the sick room. The practical importance of this is that no measure of prevention is of much value unless the patient is free from lice.

One hopes that the book will stimulate an interest in this important subject.

DISEASES OF THE EYE.—By Sir John Herbert Parsons, C.B.E., D.Sc., F.R.C.S., F.R.S. Tenth Edition. Revised with the Assistance of H. B. Stallard, M.A., M.D., F.R.C.S. 1942. J. and A. Churchill, Limited, London. Pp. viii plus 726, with 21 plates and 372 text-figures. Price, 25s.

THIS book requires little introduction; it is one of the best-known textbooks on eye diseases in the English language. The last edition appeared four years ago and much has happened since then, so that there has been considerable revision throughout. One of the most important advances has been in local anaesthesia and nerve block; and a section has been devoted to this subject, but these advances have necessitated a revision of much operative technique also.

The importance of vitamin deficiency in the aetiology of eye diseases has also received fuller recognition during the last few years, and the reviewer feels that perhaps more could have been made of this matter in this new edition.

The section on trachoma is a little disappointing. The medicinal treatment (with sulphonamides), the treatment by local applications (e.g., copper sulphate) and the operative treatment are all described, but the student will find it difficult to decide when each is to be applied. The warning not to diagnose trachoma in the well-nourished child of well-to-do parents is no doubt generally sound, but it might lead one to fail to make this diagnosis in Lady X, who had caught it from her durzie in India. And the writer's remarks about Irish and aliens might give offence in some quarters; the reviewer is himself slightly sensitive about the latter word.

These minor criticisms are the result of considerable critical scrutiny of this excellent book, and may well be ignored. The format shows little signs of the present difficult times for publishers.

TEXTBOOK OF MEDICINE.—By Various authors. Edited by J. J. Conybeare, M.C., D.M. (Oxon.), F.R.C.P. Sixth Edition. 1942. E. and S. Livingstone, Edinburgh. Pp. xx plus 1147. Illustrated. Price, 28s.; postage, 9d.

It is not unnatural that a reviewer should be influenced by the author's treatment of the subjects with which he, the reviewer, is most familiar. Twenty years ago, the majority of the standard textbooks of medicine, both British and American—perhaps the former were the worst offenders—were deplorable in their treatment of tropical diseases; information was always at least twenty years out of date and inaccurate at that. Authors are much wiser to-day; they either get these sections written by experts or at least vetted by them.

In the latest edition of this book, the chapter on tropical diseases has been contributed by Wing-Commander F. E. Lipscombe; in vain does one look for the old puerilities. Each section appears to the reviewer to be a masterpiece of compression, and very seldom does this compression lead the writer astray.

One possible example is in the typhus section, but the reviewer admits that the offending sentence gives him an opportunity to ride one of his particular hobbies:—
'*Endemic or tropical typhus* includes Brill's disease of rats in America, Palestine, Australia and South Africa; "ship fever" of dogs in several Mediterranean ports and "urban" typhus of rats in Malaya, all transmitted to man by fleas'.

Now, Brill did not describe a disease of rats but of man, and whatever view one takes of Brill's disease, that it was a mild inter-epidemic form of true typhus, or, the view expressed by Zinsser, that it was a late recurrence of typhus in an individual who had had the disease in childhood in his European country of origin, it is certainly not a disease of Palestine, Australia, or South Africa. 'Ship fever of dogs' is a wonderful confusion of ideas, ship typhus of Toulon and *fièvre boutonneuse*. There are two parts to a parasitic disease, the infecting organism and the host reaction; you can talk about a rickettsial infection of a rat or a dog, but you cannot refer to 'typhus' of rats or dogs any more than you can talk about 'typhus' of fleas or ticks. However, that is sufficient on this theme.

The other chapters are equally concise and informative. The reviewer has chosen this book as the only reference book on general medicine that he proposes to take on a two-months' sea trip on a cargo boat.

L. E. N.

AIDS TO OBSTETRICS.—By Leslie Williams, M.D., M.S., F.R.C.S. Eleventh Edition. 1942. (Students' Aids Series.) Baillière, Tindall and Cox, London. Pp. viii plus 238, with 10 illustrations. Price, 4s.

THE latest edition of this popular handbook has been revised and brought up to date, giving in a little over 200 pages all the essentials of obstetrics, including operations. The subject matter has been dealt with in a clear and concise style which will appeal to students preparing for their final examinations. It should, of course, be remembered that it is an aid and not a textbook. The volume easily slips into a pocket.

R. N. C.

TUBERCULOSIS IN CHILDHOOD.—By Dorothy Stopford-Price, M.D. (Univ. Dublin). With a Chapter on Tuberculous Orthopaedic Lesions and other contributions by Henry F. MacAuley, M.Ch., F.R.C.S.J. 1942. John Wright and Sons, Limited, Bristol. Pp. vii plus 215, with 87 illustrations. Price, 17s. 6d.

IN India, until recently, little interest was taken in the subject of childhood tuberculosis which has certain features distinct from those encountered in western countries. The more benign forms recognized in Europe and America are not so frequent here presumably because, India is less industrialized. Glandular affection is less prevalent, and bovine tuberculosis is relatively uncommon in this country. It is imperative that more attention should be paid to the subject of the incidence and the type of lesions of child tuberculosis, and that steps be taken for early detection and treatment. It is well known that many vague symptoms of ill health in children, such as loss of appetite, dyspepsia and vague pains, can be caused by tuberculous infection and indeed the disease is often mistaken for 'chill', influenza, malaria and even typhoid fever. By organizing a system of diagnosis and early treatment it is possible to reduce mortality.

Dr. Stopford-Price's book is a brief practical guide to the diagnosis and treatment of tuberculosis in children, special emphasis being laid on the pulmonary lesion. For diagnosis, considerable reliance has been placed on the cutaneous tuberculin test, the various forms of which are described in detail, and secondly on radiological appearances. There are many excellent illustrations, most of which are radiograms showing lung lesions. The author follows Ranke's classification of pulmonary tuberculosis, dividing the disease into three stages, primary, secondary and tertiary, the clinical features being described separately under each head. The value of the descriptions is enhanced by numerous

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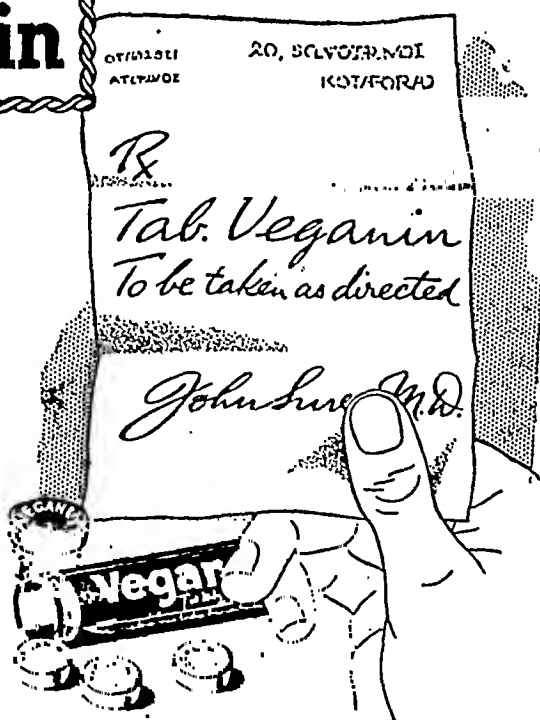
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case notes. Treatment is divided into general and specific and includes a discussion on prevention. The last two chapters are devoted to extra-pulmonary tuberculosis, e.g., of bones, eyes, glands, etc.

The book is stimulating, and is recommended to general practitioners and hospital physicians. School medical officers should also find it useful.

R. N. C.

Abstracts from Reports

REPORT OF THE SIXTY-EIGHTH YEAR'S WORK IN INDIA AND BURMA OF THE MISSION TO LEPEPERS: SEPTEMBER 1941 TO AUGUST 1942

THE work of the Mission to lepers in India and Burma during the year now reviewed cannot be described as uneventful. The service rendered at the Homes in Burma has been temporarily frustrated. In India there have been difficult periods of administration at numerous Homes. Nevertheless, at the end of the third year of the war the Mission was still caring for a large number of leper patients and providing separately for hundreds of children of leper parentage. Medical work has continued to give encouraging results.

In 1941 the total expenditure on the work in India and Burma was Rs. 7,57,653. Government and local grants came to Rs. 3,39,346, and local contributions direct to Homes totalled Rs. 17,027, leaving Rs. 4,01,280 to be provided for from Mission funds, either contributed in India or abroad.

The report includes an account of the work done in different leper Homes during the year, with special reference to their medical, social and spiritual activities.

ANNUAL REPORT OF THE DIRECTOR OF THE PASTEUR INSTITUTE OF SOUTHERN INDIA, COONOR, FOR THE YEAR 1941-42

THE Institute, since its inception in 1907, has taken an important part in medical and health work in South India. Besides anti-rabic work it provides facilities for various researches financed from different sources. In recent years the Association has also undertaken general laboratory work in response to the demands for the services of a first-class general laboratory in South India.

A total of 1,772,955 c.c.m. of anti-rabic vaccine was manufactured during the year. Altogether 249 patients received a complete course of treatment at the Institute, while 56 had incomplete courses.

During the 35-year period from 1907 to 1941, the total number of patients treated at the Institute was 38,465, among whom 395 subsequently died of rabies, giving a mortality rate of 1.03 per cent. No deaths from rabies among treated patients (complete and incomplete) were reported during the year under review.

The treatment was also given at various subsidiary centres. Out of 13,977 case cards, 10,343 received a complete course of treatment and 3,527 were incompletely treated. The remaining 107 were discharged from further treatment as the possibility of rabies in the biting animals was excluded. Only 16 deaths were recorded giving a mortality rate of 0.12 per cent.

The total number of patients treated at the subsidiary centres during the 20-year period from 1922 to 1941 was 154,155, among whom 632 deaths were reported, giving a mortality rate of 0.41 per cent.

One case of post-treatment paralysis ('paralytic accident') was reported during the year. The patient has partially recovered.

Anti-rabic vaccine was also made available for the prophylactic treatment of animals. The number of animals treated during the year was 591, of which 498 were dogs.

During the 19-year period from 1923 to 1941, 5,843 animals have received anti-rabic treatment, among which 116 deaths have been reported, giving a mortality rate of 1.98 per cent.

The Institute received 494 brains from suspected rabid animals for examination. These included 443 from dogs, of which 334 were positive.

Research work was undertaken on the effect of different vaccines on animals, including a study of the brains of various animals dying of natural or experimental rabies.

The Nutrition Research Laboratories studied the nutritive value of Indian foods. The vitamin-D content of samples of shark-liver oil has been determined. The oil is now being largely used as a substitute for cod-liver oil. Further work has been done on superficial keratitis due to riboflavin deficiency. A field enquiry on infantile beri-beri has encountered numerous cases that have been successfully treated with injections of vitamin B₁. Their clinical picture differs from the usual textbook descriptions.

In connection with malaria investigations by a unit of the International Health Division of the Rockefeller Foundation, special studies were made on immunization of fowls, determination of their spleen volume, etc. Field investigations were carried out in Pattukkottai, Tanjore district.

Correspondence

PSEUDO-TUBERCULOSIS OF THE LUNGS WITH EOSINOPHILIA

SIR,—I have read with great interest Dr. Treu's article entitled 'Pseudo-Tuberculosis of the Lungs with Eosinophilia: Contribution to Treatment' in the February number of the *Indian Medical Gazette*.

The condition he refers to appears to be fairly common in Bombay. I have seen about 35 cases in 9 years in private practice. The outstanding clinical symptom in my cases has been febrile intermittent attacks of bronchitis often with symptoms of bronchial asthma. The W.B.C. count usually ranges from 20,000 to 85,000, the eosinophile count from 25 to 82 per cent, depending upon the stage of the attack in which the patient is seen. In slides with a high eosinophile percentage, there are marked differences in the nuclei of the eosinophiles. Many are highly lobated which, in analogy to the neutrophiles, probably means that, in this disease, circulating eosinophiles reach a stage of development more advanced than that normally encountered. I believe this to be pathognomonic of the disease in question, as I have never seen such forms in eosinophilia due to other causes. I have seen many cases in which the radiological evidence is as described by Treu in his case no. 1 and by Frimodt-Møller and Barton, *Indian Medical Gazette*, October 1940. There appears to be a very fine, almost miliary, dissemination of small nodular opacities evenly distributed over both lung fields. In some cases there is no radiological evidence of pulmonary abnormality. Another symptom found in about 50 per cent of my cases is a distinct enlargement of the spleen. The clinical picture is often so characteristic that I have repeatedly been able to make the diagnosis before examining the blood-film. In a number of my cases, most detailed clinical and laboratory investigations were made to find a causative agent, but hitherto without the slightest success. I have seen cases among Europeans and Indians of all communities, the youngest being a child of 5 and the oldest 52. They were all males.

I record my cases under the diagnosis 'benign eosinophile leukaemia'. This term appears to me more suitable than either 'eosinophile lung' or 'pseudo-tuberculosis of the lung with eosinophilia'. I find the latter term particularly objectionable; firstly, because it will inevitably lead to a psychologically

wrong attitude of the patient towards the diagnosis (similar to the one we are so familiar with in cases of so-called 'pseudo-angina'); secondly, because the condition in question does not in my experience closely resemble phthisis; moreover, it appears doubtful whether the abnormality in the lung is of primary importance. The only constant factor in the disease is the hæmatological abnormality and hence the term 'benign eosinophile leukæmia' seems to me most suitable. A condition which appears to be identical with the one under discussion has been described by several French authors as a tropical disease which they call 'grande eosinophilie sanguinaire'. It does not appear to be identical with 'hereditary eosinophilia' as I have never been able to establish a hereditary factor.

After much trial and error, I have adopted treatment with arsenic, using mapharside, and have without exception had the same dramatic results as Treu. I have given mapharside taken up in 10 per cent calcium gluconate (instead of distilled water) in bi-weekly injections; 4 to 6 usually being required to bring the W.B.C. count and the eosinophile percentage to normal with complete disappearance of all clinical symptoms after the second or third injection.

While trying to find a therapeutic method, I used, among other things, liver injections, and made the peculiar observation that temperature, cough and other clinical symptoms improve while the abnormality in the blood increases. Since becoming familiar with 'benign eosinophile leukæmia' I have made it a habit to examine the blood in every case of chronic febrile cough in which tubercle bacilli are absent from the sputum.

In Bombay, some practitioners treat 'asthma' with N.A.B. injections and claim very good results in some cases. I am tempted to think that these may have been cases of 'benign eosinophile leukæmia', as the pulmonary symptoms often resemble asthma very closely.

Although a number of cases came to me in a deplorable general condition, I have never seen a fatal case even in the days before I adopted treatment with arsenicals. The continued observation of untreated cases shows that the condition gradually appears to improve spontaneously, the blood findings, however, never becoming normal; and then, for no apparent reason, exacerbations occur, sometimes at intervals of years. Since adopting treatment with mapharside I have never seen a relapse. This disease appears well worthy of further investigation.

A. T. W. SIMEONS, M.D.,
Medical Officer In-Charge,
Satara Camp.

THE MALL,
SATARA,
5th March, 1943.

AMŒBIC DYSENTERY

SIR,—In your Editorial article on 'Amœbic Dysentery as a Water-borne Disease' in the *Indian Medical Gazette* of February 1943, you have mentioned that before the last world-war, 'the textbooks stressed the fact that amœbic was the dysentery of the tropics while bacillary had a more universal distribution', with the result that in the tropics 'all dysenteries were thought to be amœbic and usually treated as such'. But 'it was later found that in many war theatres, about 90 per cent of the dysenteries were really bacillary and for the last twenty years the textbooks . . . have been rubbing in this fact'. But 'the present indications are that in the majority of cases the dysentery among the troops, at any rate the British troops, in India to-day is amœbic'.

What can be the explanation of this? Has there been any real change in the relative frequency of the two types, during the pre-war, post-war and the present periods? Is this merely an instance of change of fashion in diagnosis; is it due to wrong generalizations from observations in a limited field under special conditions?

The writer made careful observations for some years on cases coming under his care in the Osmania Hospital, with a view to finding out the relative prevalence of the two types. In his annual report to the Superintendent for 1342 Fashi (October 1932 to September 1933) the writer stated, 'Our figures, small as they are, appear to be definitely against the findings of other investigators mentioned by Acton and Knowles (1928), who state that amœbic infections form only about 20 per cent of all cases of dysentery'. Observations during subsequent years—when male cases of dysentery were to some extent concentrated under the writer's care—confirmed this opinion.

Below are given the figures for four years 1342–1345 :—

Figures showing cases of dysentery (males only) treated during the years 1342–1345 Fashi (October 1932 to September 1936).—

Year	Total number	Bacillary	Amœbic	Mixed	Indefinite
1342	40	..	18
1343	72	9	36	3	24
1344	81	13	37	..	31
1345	71	18	33	..	20
GRAND TOTAL.	264	40	124	3	75
PERCENTAGE.	100	15.4	46.94	1.14	28.4
			48.08		

The patients were practically all adults from the poor or lower middle class of the civil population admitted for treatment as in-patients.

No case was diagnosed as amœbic without finding living moving amœbæ containing red blood corpuscles in a smear preparation of the fresh stool or material obtained on protoscopic examination. Cultural and serologic methods were not available; a case was classed as bacillary when the microscopic characters of the stool were typical, and as indefinite under other conditions.

It is almost certain that this last group included some cases which were not dysentery. Yet the table shows that not less than 48 per cent of our 264 cases were amœbic; and if all cases not dysentery could be excluded, the percentage of amœbic cases would rise higher.

REFERENCE

ACTON, H. W., and *Dysenteries of India*. Thacker, Knowles, R. (1928). Spink & Co., Ltd., Calcutta, pp. 20–22.

S. W. HARDIKAR,
Professor of Pharmacology and
Honorary Physician, Osmania Hospital.

HYDERABAD DECCAN,
23rd March, 1943.

[Note.—It is probably true that in hospital in-patients, amœbic dysentery is often more common than bacillary dysentery, but this fact does not prove that the same is true in the general population or in troops, British or Indian. Also it appears more than probable that in the damper parts of the tropics, amœbic dysentery is more common than in the dryer and often hotter parts of the tropics and sub-tropics. We agree with Dr. Hardikar that there is no rule in these matters, and that each outbreak, and if possible each case, needs thorough examination and proper classification as amœbic or bacillary. One has so often seen cases of bacillary dysentery persistently treated with emetine, and showing little or no improvement, but definite signs of emetine poisoning.—EDITOR, I. M. G.]

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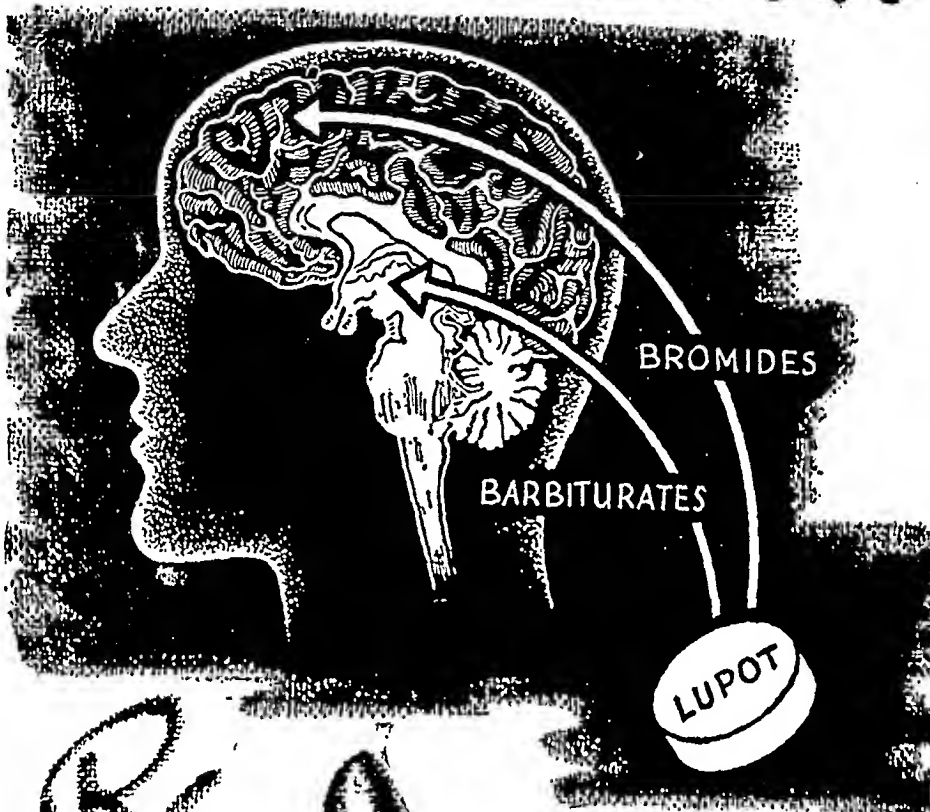
emerged as 'the most effective stimulant.' Briefly, it was proved that Bovril increased the supply of gastric juices where there was a deficiency and restored it to normal. It is an accepted medical fact that people of sedentary habits generally suffer from a lowering of the essential gastric activity; Bovril rectifies this and, by facilitating the digestion of proteins, enables full nourishment to be gained.

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Service Notes

APPOINTMENTS AND TRANSFERS

MAJOR R. I. REID is appointed Deputy Director of Production (Instruments and Appliances) in the Stores Section of the office of the Director-General, Indian Medical Service, with effect from the 9th January, 1943.

INDIAN LAND FORCES (Emergency Commissions)

To be Majors

Shiv Das Suri. Dated 5th February, 1943.
Gurdas Ram Charnalia. Dated 6th February, 1943.

To be Captains

Ajit Kumar Basu. Dated 1st January, 1943.
Mohammad Mohsin. Dated 4th January, 1943.
Mohan Lal Das. Dated 5th January, 1943.
Subodh Chandra Kundu. Dated 7th January, 1943.
Abdur Rahman Mahmood Pesh-Imam. Dated 9th January, 1943.
Hari Nandan Sahay. Dated 10th January, 1943.
Udamalpet Viswanathaiyar Srikanteswaran. Dated 22nd January, 1943.
Pran Kumar Guha. Dated 24th January, 1943.
Choyi Raman. Dated 27th January, 1943.
Methil Achutan Nair. Dated 1st February, 1943.
Adige Gopalkrishna Rao. Dated 3rd February, 1943.
Muhamad Abdul Hamid. Dated 4th February, 1943.

5th February, 1943

Damerla Veer Raja Rao. Michael Colaco.
Bisheshwar Prasad Srivas- Victorine Caetano Garlos
tava. Francisco Junot Faria.
Dhirendra Kumar Guha. Amalendu Chatteraj.
Birinchibilas Ray. Abdul Ghafur.
Dorab Billimoria. Dated 6th February, 1943.
Yellore Raju Shetty. Dated 8th February, 1943.

The undermentioned Captains are transferred to the General Service cadre with effect from the dates shown against each :—

INDIAN LAND FORCES (Emergency Commissions)

S. N. Ray. Dated 10th November, 1942.
P. R. Solanki. Dated 14th December, 1942.
S. A. Rahim. Dated 24th December, 1942.
V. C. Kamaraju. Dated 4th January, 1943.

To be Captains

20th September, 1942

J. G. Bentley. John Wilfrid Brown.
Leopold Noel O'Hara. Dated 15th January, 1943.
(Miss) Berenice Criouleansky. Dated 26th January, 1943.
Bimal Chandra Chatterjee. Dated 28th January, 1943.
Tribidish Roy. Dated 4th February, 1943.

5th February, 1943

Mohammad Afzal Sheikh. Basanta Kumar Aikat.
(Within Indian Limits)

To be Captains

Ramaswamier Vankatachalapathi. Dated 8th January, 1943.
Subrata Chandra Mujumder. Dated 12th January, 1943.

5th February, 1943

Dhirendra Nath De. Subal Chandra Ghosh.
Surendra Pratap Sinha.

Marinho De Azavedo. Dated 8th February, 1943.
Ajit Kumar Ghosh. Dated 5th February, 1943.
Girijakanta Chakravarty. Dated 23rd February, 1943.

The undermentioned Officers are transferred to the General Service cadre with effect from the dates shown against each :—

INDIAN LAND FORCES (Emergency Commissions)

Captains

L. Narayan. Dated 1st December, 1942.
N. G. Rajulu. Dated 8th January, 1943.
N. Choudhury. Dated 23rd January, 1943.

Lieutenants

S. C. Vij. Dated 7th December, 1942.
A. H. Khokhar. Dated 1st January, 1943.
S. V. S. Krishnan. Dated 13th January, 1943.
R. Krishna. Dated 29th January, 1943.

5th March, 1942

A. Narasimham. S. D. Sikand.
M. L. Sudan.

H. A. Press. Dated 6th April, 1942.

(Emergency Commissions)

To be Lieutenants

5th September, 1942

Jogindar Singh Grewal. Asirvatham Edwin Sundareson.
Rustam Ali Nabi. Dated 14th November, 1942.
Jitendra Nath Dutt. Dated 16th November, 1942.
Narayan Vasudeo Nene. Dated 21st November, 1942.
Salahuddin Ahmad Mallick. Dated 22nd November, 1942.
Mohd. Mohsin. Dated 23rd November, 1942.
Keshab Chandra Das Gupta. Dated 26th November, 1942.
Ranjit Kumar Ghosh. Dated 28th November, 1942.
Harold James Brown. Dated 8th December, 1942.
Rabindra Nath Mitra. Dated 10th December, 1942.
Sambhu Nath Chatterjee. Dated 11th December, 1942.
Joseph Moolalaparakel Thomas. Dated 19th December, 1942.

28th December, 1942

Amarendra Mohan Roy. Ramendra Kumar Das.
Colin Douglas Torpy. Dated 5th February, 1943.
Derrick Cecil Mayberry. Dated 6th February, 1943.
Cheeren Verghese David. Dated 8th January, 1943.
Vyasarpadi Loganathan Srinivasan. Dated 9th January, 1943.
Eric Ronald MacFarlane. Dated 21st January, 1943.
Frederick George Orton. Dated 25th January, 1943.

To be Lieutenants

8th January, 1943

Arul Savarirayan Manuel.
Trichy Ramaswamy Iyer Subramanian.
Vellore Veraswamy Mudaliar Sreenivasa Mudali.
Sachindra Kumar Bhattacharya. Dated 18th January, 1943.

21st January, 1943

Hirendra Nath Sadhu. Nripendra Nath Das.

22nd January, 1943

Prithwish Chandra Sarkar.
Gopal Chandra Sen Gupta.
Ufulla Kumar Das Gupta.

5th February, 1943

Provat Kumar Mookherjee.
Laxman Dattatraya Kale.
Arvind Moreswar Sharangpani.
Kannanganatt Raman Kunjan.
Vasant Bapuji Tawadey.
Madigubba Ramachandra Rao.
Sunkara Ramachandra Rao.
Jayanty Suryanarayana Rao.
Sudhansu Bhushan Palit. Dated 6th February, 1943.
Saroj Kumar Mukherjee. Dated 8th February, 1943.

3rd February, 1943

Sudhindra Nath Basu.
Nripendra Nath Chatterjee.

15th February, 1943

Subodh Chandra Bhattacharyya.
Anil Chandra Sarkar.

18th February, 1943

Gurbakhsh Singh Grewal. Altaf Mahmood.
Abdul Majid. Balwant Singh.
Satya Prakash. Allaud Din.
Muhammad Hussain. Gurbachan Singh Athwal.
Qamar. Jemi H. F. Manekshaw.

Attar Singh Nagpal.

Velembore Loganatha Raja. Dated 4th February, 1943.

Narendra Jagmohandas Choksey. Dated 9th January, 1943.

(Women's Branch)

To be Lieutenant

(Miss) Swarn Lata Bhatia. Dated 18th February, 1943.

PROMOTIONS

Colonel to be Major-General

J. S. S. Martin. Dated 6th March, 1943.

Majors to be Lieutenant-Colonels

1st February, 1943

G. M. Irvine. D. Kelly.
S. D. Gupta. Dated 7th February, 1943.

Captains to be Majors

1st February, 1943

G. S. N. Hughes. A. D. Barber.

5th February, 1943

T. K. White. C. J. Hassett.
W. G. Kennedy. Dated 19th February, 1943.

The undermentioned officers are confirmed in their rank with effect from the dates specified :—

Captains

I. Singh. Dated 4th November, 1941.
N. A. Subramanyam. Dated 5th December, 1941.
S. C. Banerji. Dated 5th February, 1942.
K. S. Jolly. Dated 23rd February, 1942.

5th March, 1942

N. Subramanyan. B. R. Joshi.
S. Sankaran. M. Ahmad.
V. S. Bhattal. L. R. S. Deo.
T. M. Mathew. K. N. Gubbar.
N. B. Banerjee. M. N. Hukku.
M. Ray. K. R. Unger.
A. N. Das Gupta. S. C. Driver.
A. K. Ray. H. Chatterjie.
R. C. Mitra. F. N. Kapadia.
M. G. K. Menon. A. Kidvai.

M. S. Babbar.

6th March, 1942

A. K. Nandi. N. H. Oonvala.
S. C. Lahiri. D. B. Parakh.
H. B. Mallick.

7th March, 1942

K. N. Tandon. M. M. A. Jabbar.
S. P. Chatterjee. Dated 8th March, 1942.
T. M. Nair. Dated 12th March, 1942.

13th March, 1942

P. B. Kurup. M. U. Hyat.

6th April, 1942

D. G. Karandikar. S. N. Das.
K. B. Chowdhury. A. Haq.
K. R. Madhavan. B. G. Sarnabat.
S. K. Nandy. J. K. Adranvala.
B. B. Sarkar. J. R. Shah.
K. S. Srinivas. M. Habibullah.
M. S. Datta. S. G. Sidenur.
S. C. Sen Gupta. H. K. Mallick.
P. K. Dhar. B. R. Irani.
S. Ray. L. K. Kale.
T. J. Gupta. D. V. Bapat.
S. Saha. S. Y. Torne.
S. B. Jathar. J. P. Chothia.

7th April, 1942

J. N. Das Gupta. N. C. Datta.
C. J. Pinto. V. G. Hate.
H. D. Mukherjee. Dated 8th April, 1942.
V. G. Dhabolkar. Dated 18th April, 1942.
M. K. Mitra. Dated 27th April, 1942.

LAND FORCES

(Emergency Commissions)

Lieutenants to be Captains

S. McClatchie. Dated 11th May, 1942.
B. Fife. Dated 7th July, 1942.
K. N. P. S. Pillai. Dated 8th July, 1942.
A. K. Das Gupta. Dated 20th October, 1942.
P. Chandra. Dated 6th November, 1942.
N. C. Ray. Dated 19th November, 1942.
A. S. Reilly. Dated 5th December, 1942.
P. K. Basu. Dated 25th December, 1942.
K. K. Guha. Dated 23rd February, 1943.
(Miss) D. Pacheco. Dated 3rd November, 1942.
J. F. Guerra. Dated 13th December, 1942.

RETIREMENT

Lieutenant-Colonel W. M. Will. Dated 18th February, 1943.

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Original Articles

GAS GANGRENE

By RICHARD E. STRAIN, M.C.P.S. (Manitoba),
M.D. (Vanderbilt), M.C.C. (Canada)

MAISONNEUVE (1853) is generally supposed to have first identified gas gangrene. Killett (1939) discovered a letter written by Fabricius Hildanus to Gregorius Horstius in August 1607 describing a case of gas gangrene in a farmer run over three days previously by a cart which lacerated the left leg. 'I found the whole of the leg below the knee gangrenous. Furthermore, as I began to shave off some of the hair above the knee, on the outer aspect at a certain place I could make out a sound as if there were some empty space underneath.' Gangrene of the groin and scrotum developed rapidly and the patient died a day after the onset of gangrene.

Not all cases of gangrene associated with gas in the tissues are as virulent as this case of Hildanus', as is easily seen by the case I wish to report. Inability to differentiate virulent from non-virulent types has doubtless led to confusion regarding the efficacy of therapeutic measures. Toxins are thought by some to be responsible for muscle destruction and gangrene; Homans (1940) thinks that gas formed by toxins causes separation of individual muscle fibres, and that the swelling consequent upon these factors compresses adjacent blood vessels, and causes destruction of muscle tissue. *B. coli* will frequently produce gas in tissue (Scuderi, 1940, Olsson, 1939, Gillies, 1941); most of the cases reported are in diabetics. The following report of a case of gangrene of the arm with gas in the chest wall, and a brief review of recent literature seems timely, as the mortality of gas gangrene is reported as 48 per cent (Bowen, 1940).

Case report

H. N. K., a 22-year-old farmer, was admitted to Miraj Medical Centre on 4th January, 1942, complaining of gangrene of the right forearm. Eight days before admission, the patient had fallen from a platform five feet high located in a grain field, and suffered a two-inch laceration on the flexor surface of the distal part of the forearm, without injury to bone. The wound was covered with a rag; three hours later, pulp from a green coconut was bound over the wound. The second day, a 'chilly' sensation was experienced for half an hour, but no fever was noted and he continued to work. Pain and swelling gradually increased, and by the fourth day the hand began to turn black and 'shrivel up'. Discoloration progressed to the elbow, while swelling was noted to the shoulder joint. Figure 1 (plate XIII) shows the condition soon after admission. Some swelling present in the upper arm is obscured by shadow.

The temperature was 99.6; pulse 96; respiration 24. Definite crepitation was present in the upper arm, axilla and lateral to the scapula down the chest wall in the mid-axillary line to the 6th rib. Odour was slight. Smears from wet, necrotic tissue at the elbow revealed a gram-positive, encapsulated bacillus resembling *Cl. welchii*. A similar organism was grown from blood cultures both anaerobically and aerobically. Hæmoglobin was 69 per cent (14.5 grams 100 per cent); 4.01 million red blood cells; 8,000 leukocytes with 3 per cent 'stab' forms; 60 per cent segmented; 3 per cent monocytes and 34 per cent lymphocytes. Urine was alkaline with a specific gravity of 1.0200.

Oxygen by nasal catheter—60 bubbles per minute—was started at once and increased to 120 bubbles per minute after 12 hours. Five grams of sulphanilamide with one gram of soda was given; one gram of sulphanilamide with soda 0.3 gram was then given each four hours, day and night, for six days. Tetanus anti-toxin was not then available nor was gas gangrene serum in stock. Under these conditions it was decided to try the effects of x-rays, as suggestive evidence of its value exists.

Following a blood plasma transfusion of 450 c.cm., the film seen in figure 3 (plate XIII) was taken. A marked amount of gas is seen about the entire shaft of the humerus extending through the axilla above the scapula and down the chest wall as low as the 7th rib. The patient was then given 100 r to the entire right arm and chest—this was given once daily for five days.

Four days after admission, after 3 x-ray treatments and 18 grams of sulphanilamide, the swelling of the upper arm was markedly decreased. Crepitation could no longer be felt on the chest wall, and only slightly on the lateral aspect of the upper arm. Figure 4 (plate XIII) taken at this time showed a marked decrease in the amount of gas present in the tissue. The leukocytes then numbered 11,100, with 3 per cent 'stab' forms; 75 per cent segmented; 1 per cent monocytes; 20 per cent lymphocytes and 1 per cent eosinophils. Hæmoglobin was 68 per cent.

The patient gradually improved; pain was marked at the elbow; the pulse rate, taken at two-hour intervals, had never been over 106, and averaged 94 to 96 during the day and 82 to 84 at night. No photo-sensitization of skin to sulphanilamide and x-rays was observed. Figure 2 (plate XIII) shows the decrease in swelling and the beginning line of demarcation at the elbow six days after admission.

Ten days after admission and eighteen days after injury, the patient first complained of slight stiffness of the jaws, and could open his mouth only one half inch. Three thousand units of tetanus anti-toxin was given after skin testing; no more anti-toxin was available. A guillotine amputation three inches above the elbow was done through normal-looking tissue on the 14th. Sulphanilamide powder was placed on the stump and light traction was applied. The patient took

fluids well by mouth, but developed convulsions and slight opisthotonus unrelieved by 10 per cent magnesium sulphate given intravenously or sodium amytal by rectum. From the next day, respiratory difficulty was marked, and a day later the attendant is said to have poured water in the sleeping patient's mouth while the nurse was out of the room; death followed in one and a half hours.

In this instance, the response of the gangrene with gas in the tissue to a combination of oxygen, sulphanilamide and x-ray was most satisfactory, as evidenced by the marked decrease in the swelling and crepitation, and decrease in gas as seen by x-rays. The prevention and treatment of tetanus was not adequate, due to conditions over which we, at present, have no control. The causative organism was not definitely identified; it looked like *Cl. welchii*, but showed growth under aerobic conditions. Gas at a distance in this case did not mean that that area was infected. This idea is certainly contrary to the view of older surgeons, who amputated above the area of crepitation, but it is in line with recent statements.

Discussion

A number of discussions of treatment of gas gangrene are available, but it is interesting that none of them mentions or emphasizes the use of oxygen. For treatment, and also prophylaxis, the following are available: anti-toxin; transfusion or complement; sulphonamide; x-rays; oxygen and surgery. Usually a combination of these methods will give the best results.

Anti-toxin, as Miles (1941) emphasizes, is species-specific only; therefore, identification of organisms involved is essential. In practice, a polyvalent anti-toxin is used; for established cases, the War Wounds Committee of the Medical Research Council recommends anti-toxin given intravenously as soon as possible, 7,500 international units of *Cl. welchii*; 3,750 units of *Cl. septique*; 2,500 units of *Cl. oedematis* repeated as necessary, plus chemotherapy. It is thought that serum has some value in limiting spread (Editorial, 1940); its administration in the form of multiple injections of serum into muscle in the vicinity of the wound is recommended by Gordon and McLeod (1941).

For prophylaxis, the value of anti-toxin is not proven. Gordon and McLeod urge that the official recommendation to use anti-toxin for treatment only should be withdrawn. Craig (1938) reports 13 cases of gas gangrene in 4 of which gangrene developed after prophylactic doses of 10,000 to 20,000 units. Maecy (1939) reports a case of gas gangrene developing after the administration of 20,000 units of polyvalent perfringes anti-toxin and after surgical measures adopted within two hours of injury. Perfringes anti-toxin controlled the infection after 4 grams daily of sulphanilamide failed to do so. The recommended dose of anti-toxin given prophylactically has been 1,500 units.

Sulphonamides. In treatment.—Bohlman (1937) successfully treated the first cases (Seuderi, 1940, Olsson, 1939, Gillies, 1941) with sulphanilamide combined with sensible, conservative surgery. Love (1940) reported excellent results from treatment with sulphapyridine combined with surgical measures used without delay to remove foreign bodies and to secure drainage. An editorial (Editorial, 1940) states that drugs of the sulphonamide group in large doses are certainly of much help; but, in the main, good results seem to have been obtained in relatively superficial injuries. The War Wounds Committee of the Medical Research Council recommends sulphanilamide plus anti-toxin and conservative surgery for established cases. Sulphanilamide is given, 2 grams the first dose—subsequent doses 1 gram starting two hours later and continuing four-hourly for two days. After the first two days, the dosage is gradually reduced as the condition improves. Small doses, 3 grams daily, should be given for three to four days after the temperature is normal, and the total dosage should not exceed 35 grams.

In prophylaxis.—Numerous reports show that sulphonamides are of limited value in preventing gas gangrene. Bliss *et al.* (1939) and Stephenson and Ross (1940) showed that mice were protected against lethal intra-peritoneal doses. Bonnin and Fenner (1941) recommended the application of 20 grams locally after injury. Reed and Orr (Reed and Orr, 1941) in guinea-pigs showed that in animals infected with *Cl. welchii*, *Cl. septique*, *Cl. sordellii* and *Cl. novyi*, oral treatment saved 25 per cent; local treatment 55 per cent; combined oral and local treatment 44 per cent. Sulphathiazole was most effective, with 87 per cent survivals; sulphapyridine was more effective than sulphanilamide. Kropp and Smith (1941) found that sulphanilamide overcame the inhibitory action of the infection on the migration of leukocytes and phagocytic cells. The War Wounds Committee recommends for prophylaxis that excision of contaminated war wounds be done at the earliest opportunity, and be combined with chemotherapy.

Lockwood (1940) points out that experimentally infected subcutaneous and intra-peritoneal wounds are quite different from clinical gas gangrene where infection is primarily in devitalized muscle. He states that when bacteria are introduced intramuscularly, even after having been washed free from preformed toxin, no protection has been afforded by the sulphonamides. Kendrick (1939) had previously reached this conclusion. Caldwell (1941) found that sulphanilamide crystals in experimental compound fractures infected with *Cl. welchii* did not control or prevent gangrene. X-rays were also ineffective. Gordon and McLeod (1941) introduced organisms into artificially damaged limbs with a syringe (probably into muscle) and found that the sulphonamide drugs have only a limited value in prophylaxis, and that local application is more

useful than oral. They conclude that drugs are not likely to be of value except when there is a mixed infection with aerobes susceptible to them.

The mode of action of the sulphonamides is obscure. It is known that necrotic tissue contains sulphonamide inhibitors, para-aminobenzoic acid being one; therefore removal of devitalized tissue would seem essential.

Miles (1941) states both leukocytes and complement contribute to the effect of the sulphonamides. He further emphasizes that the combination of anti-toxin and toxin, by fixing some of the complement, impairs the efficiency of the natural anti-bacterial mechanism. The value of renewing complement by transfusion is obvious; it is not so clear how valuable stored blood would be in restoring complement.

There is some evidence (Mayo and Miller, 1940) that sulphonamides are more effective where oxygen is abundant. As Barach (1939) points out 'at 50 to 60 per cent oxygen concentration in inspired air, there is an increase of two and one half to three times the normally physically dissolved oxygen. Furthermore, the haemoglobin, even of a normal individual, can be additionally saturated by 5 per cent. The summation of these two influences will increase the oxygen content in 100 c.cm. of blood by almost 2 c.cm. Since from 4 to 6 c.cm. of oxygen is consumed in 100 c.cm. of blood as it passes from artery to vein, an increase of 2 c.cm. has considerable physiologic significance'. Boothby *et al.* (1940) with a forked nasal-tube flow of 2 litres of oxygen per minute, found that dry alveolar air contains 42 per cent oxygen; with a flow of 4 litres per minute—50 per cent oxygen; with a B.L.B. mask this is increased to 70 to 85 per cent at 4 litres per minute. One would expect that any increase in oxygen in the tissue would aid in combating anaerobic organisms provided that it can reach them.

Kelly *et al.* (1938) has treated 143 cases with x-ray since 1928 without a death. Williams and Hartzell (1939) analyse 34 cases. In 12 control traumatic cases, 7 patients died; 4 lost a leg; 1 had severe contractures. In a similar series treated by x-rays only 1 died.

Godby (1940) treated 5 cases with x-rays. Three patients were considered too ill for intervention; one was moribund and died. In 3 cases serum and prontosil had been given. Four cases lived. Sewell (1940) treated a severe case involving the trunk in which irradiation was apparently the prime factor in recovery. Coleman and Bennett (1939) used x-rays alone on 14 cases out of 41 which were thought to be too sick for surgery. Ten died—all had septicaemia. Four responded to x-rays; wide opening and amputation resulted in recovery. They believe that scrotherapy and roentgen therapy are not of real value unless proper surgery has been done early.

Bowen (1940) says that experimental work indicates that hydrogen peroxide is produced in tissues by the action of x-rays. Again, the

administration of oxygen would seem indicated to aid in producing more hydrogen peroxide. de Lorimier (1941) points out that the United States Army is preparing to treat potentially infected cases with low voltage x-rays. This can be done with a diagnostic or portable unit; 90 to 100 kv. is recommended (Bowen, 1940) for the extremities; 130 to 160 kv. on the trunk; 100 r per dose per field is given. About 6 treatments, two daily, are required. Occasionally 50 r daily for a few days more may be required.

One cannot emphasize too strongly that none of the previous measures discussed will displace sensible, conservative surgery but they are to be used in conjunction with surgery.

In prophylaxis, damaged tissue should be removed and sulphonamides packed into the wound, sulphathiazole being the most effective. There is some evidence that closure of the wound may not always be contra-indicated.

In treatment, it is essential that the wound be opened up and that devitalized muscle be excised. Devitalized muscle inhibits sulphonamides (which should be placed in the wound); such muscle cannot regenerate and moreover provides a medium of growth of organisms. The presence of gas at a distance does not mean that muscle there is devitalized or even infected; therefore, radical amputations are no longer justifiable.

Summary

The value of oxygen as an adjuvant in anaerobic infections has been neglected. On theoretical evidence available, the use of oxygen would appear logical in gas gangrene, in that it increases the amount of oxygen in tissue two or three times. There is suggestive evidence that this increase in oxygen may aid the effect of the sulphonamides.

X-rays, by liberating hydrogen peroxide in tissue, have proved of definite value in cases of gangrene with gas. An ordinary diagnostic or portable unit may be used, and such a unit has been adopted by the United States Army for this purpose.

Anti-toxin is species-specific only, and requires complement to neutralize toxin. In treatment, a polyvalent serum injected intravenously and around the wound into muscle should be given as needed. The prophylaxis by anti-toxin is uncertain.

Sulphonamides should be given in every case of gas gangrene, potential or established. Sulphathiazole is most effective. Local application is most effective. Cases of gangrene with gas caused by aerobic organisms appear sometimes to be cured by sulphonamides alone.

Sensible, conservative surgical procedures—namely, the excision of severely damaged and devitalized tissue—should be practised in all cases of gas gangrene, potential or established. This should be done as early as possible. The presence of gas at a distance does not mean that

the tissue of that area is devitalized or even infected, so radical amputation is not justifiable in such cases.

A mild case of gas gangrene of the arm with gas involving the trunk, associated with septicaemia responded to oxygen, plasma transfusion, sulphanilamide and x-ray.

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PANCREATIC CYST TREATED BY PRIMARY ANASTOMOSIS TO THE STOMACH

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THE accepted treatment of cysts of the pancreas has been either removal when possible, or marsupialization by suturing the cyst wall to the anterior abdominal wall, with evacuation and drainage. The former is not often practicable because of the extensive adhesions to vital parts, and because of the large blood vessels in and around the cyst. Cysts in the tail of the pancreas are occasionally suitable for complete extirpation. Consequently, except in a few cases, marsupialization has been the operation of choice. It was first performed in 1882 by Gussenbauer, a pupil of Billroth. He devised a method of drainage whereby he sewed the parietal peritoneum to the skin, and the walls of the cyst to the parietal peritoneum. Marsupialization thereafter became and has remained a standard surgical procedure (Judd *et al.*, 1931). The object of this paper is to show that the best treatment may be primary anastomosis to the stomach, duodenum or jejunum, and that this is usually possible. The operation of marsupialization has several disadvantages, and consequently should, in the opinion of writer, give place to this procedure of primary anastomosis to the stomach, duodenum or jejunum.

Case report

K. R., male Hindu, aged 30 years, a carpenter, was admitted on 1st June, 1942, with a moderately large and obvious epigastric swelling. The trouble started quite suddenly during a meal 20 days before admission. There was epigastric pain shooting to the back; and a sensation as if a swelling was appearing in the epigastrium. The patient vomited, but the pain persisted for a week, by which time he noticed the swelling. He also noticed that after that, the swelling disappeared every 3 or 4 days, only to reappear again. He became very constipated and the appetite became poor.

Examination showed a tense, elastic, cystic swelling in the epigastrium, extending from the xiphisternum to just above the umbilicus, and from the rectus border on one side to the rectus border on the other, freely moving with respiration, moving from side to side as well as from above downwards, dull to percussion and tender to palpation. The tumour dullness was not continuous with liver dullness. There was no free fluid in the abdomen. The next day (2nd June, 1942) the tumour disappeared quite completely. The epigastric region however was tender, and the patient was distinctly uncomfortable. There was no question of the tumour being masked by a tense abdominal wall, because the area was now quite resonant. Within the next 3 days the tumour became evident, and in another 3 days (8th June, 1942) had become very large and tense, even larger than before. The next day (9th June, 1942) it disappeared again and the patient felt more ill, and had audible gurgling sounds and epigastric tenderness. The tumour reappeared in another 3 days (12th June, 1942) to disappear again (16th June, 1942). It again became obvious in another 4 days, and in the course of a week reached the big size already noted. Thereafter it persisted.

PLATE XIII
GAS GANGRENE : R. E. STRAIN



Fig. 1.—Condition soon after admission. Swelling of the upper arm is obscured by shadow.



Fig. 3.—Note the large amount of gas surrounding the shaft of the humerus and extending through the axillæ and down the chest wall to the seventh rib.



Fig. 2.—After five days of treatment with oxygen, sulphanilamide and x-ray. Note the decrease in swelling of the upper arm.



Fig. 4.—Note the marked decrease in the amount of gas about the shaft of the humerus after three days' treatment. Gas has practically disappeared from the chest wall.

PLATE XIV
PANCREATIC CYST TREATED BY PRIMARY ANASTOMOSIS TO THE STOMACH :
R. MAHADEVAN



Fig. 1.



Fig. 2.

Showing typical filling defect of stomach due to extra-mural pressure; barium meal pictures at 5 minutes' and 1½ hours' interval.

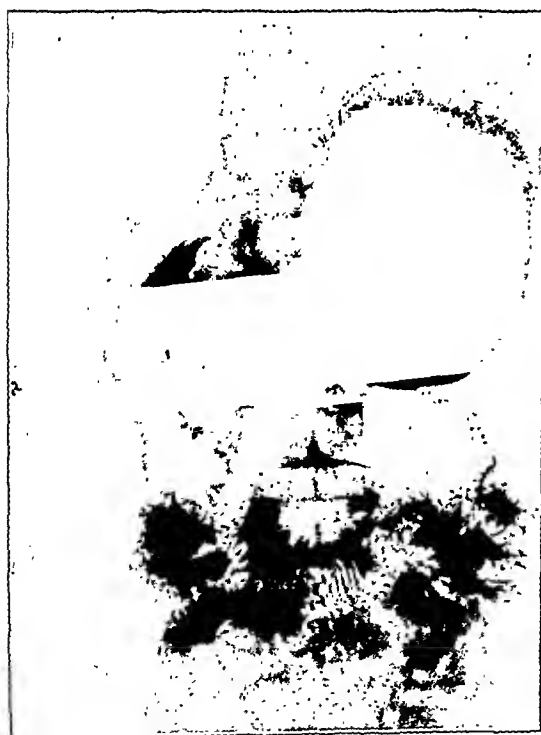


Fig. 3.

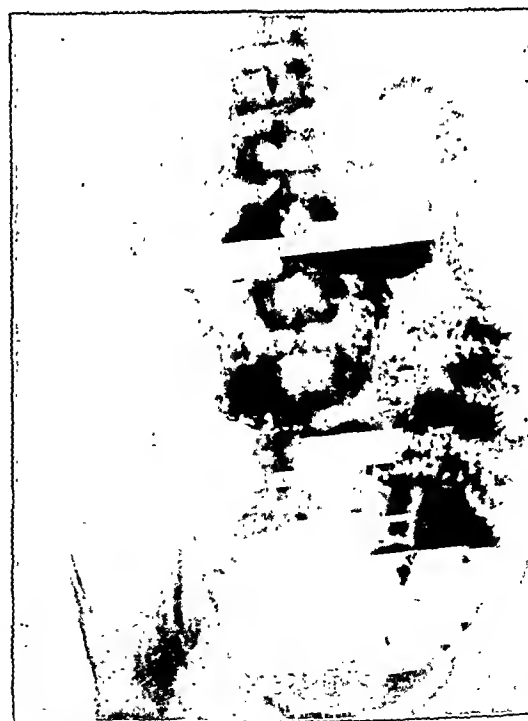


Fig. 4.

Showing barium meal picture of stomach after operation, at 5 minutes' and 1½ hours' interval. Note that the filling defect has now completely disappeared.

One interesting feature was that the tumour was at a higher level when he was in the erect posture than when he was recumbent. This is quite contrary to the usual finding.

The patient was fairly well nourished, of thin build, and weighed 80 lb. The urine contained no albumin or sugar. The diastase test showed 100 units. The stool showed no ova or cysts, and no undigested muscle fibre. The fat in the stools was normal. The haemoglobin was 80 per cent; the R.B.C. count was 6,285,000; the W.B.C. count was 4,200; the Van den Berg test, direct delayed positive and indirect positive; the plasma bilirubin was 1.8 units; and the Wassermann reaction was negative. The barium-meal picture showed a big and typical filling defect due to extramural pressure (see table XIV, figures 1 and 2). Fractional test meal curves are shown in figures 5, 6 and 7. A pyelogram showed normal kidneys and pelvises.

Fractional test meal curve.

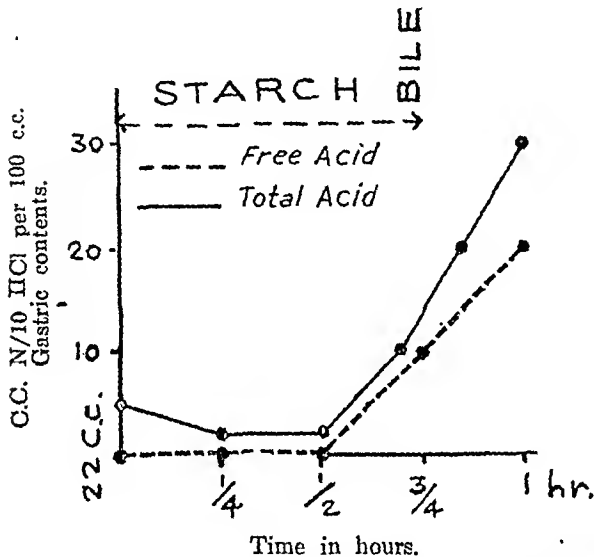


Fig. 5.—Pre-operative curve. 11-6-42.

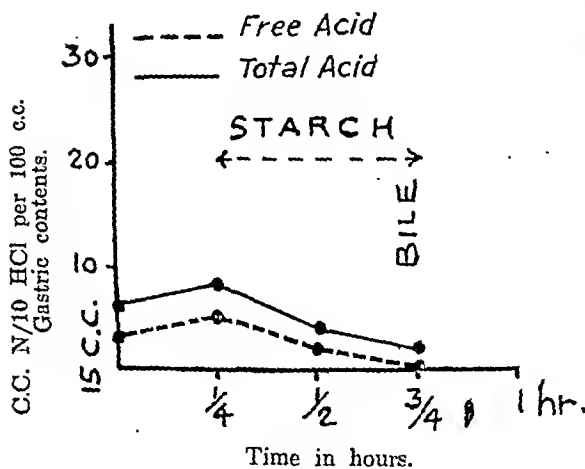


Fig. 6.—Post-operative curve. 28-8-42.

Operation findings

Operation performed on 30 June, 1942, under spinal anaesthesia, by a median supra-umbilical incision, revealed a tense cystic swelling extending from the under surface of the liver to well below the transverse colon. The lesser omentum, stomach, transverse colon and its mesocolon were stretched out in front of it, the stomach being

spread out in front of the mid-portion of the cyst. Further examination was possible only after tapping the cyst, when 17 oz. of slightly blood-stained fluid were withdrawn. The cyst was now found to be adherent to the under surface of the liver, the posterior part of the stomach, and the transverse mesocolon. The pancreas could be felt behind the cyst, to which it was very adherent, and felt hard and somewhat nodular. There was a small calcareous plaque in the anterior wall of the cyst. The gall-bladder was normal in size, and could be emptied easily; no stones were felt. Its wall was slightly opaque.

After carefully packing off the general peritoneal cavity, an incision was made in the long axis and on the anterior surface of the stomach and to the left of the pyloric part, in front of which the cyst was protruding most. In a convenient area surrounded by a purse string suture, a small nick was made into the anterior wall of the cyst. By introducing the index finger through this opening, an area where the cyst was adherent to the posterior stomach wall and free from big blood vessels was evaginated towards the incision in the anterior stomach wall. With a long artery forceps guided along the finger, this area was kept taut, a 3- to 4-inch incision was made with the diathermy knife through the thickness of the tissues, and the cyst was laid open into the stomach. The margins of this opening in the cyst and posterior stomach wall were sutured together to ensure that they would not tear apart when allowed to fall back into place. During this process, about 3 ounces of fluid escaped into the stomach. The openings in the stomach wall and cyst were closed, and the area of the incision in the cyst was covered over with omentum. A 'stab' drain was drawn through the left loin

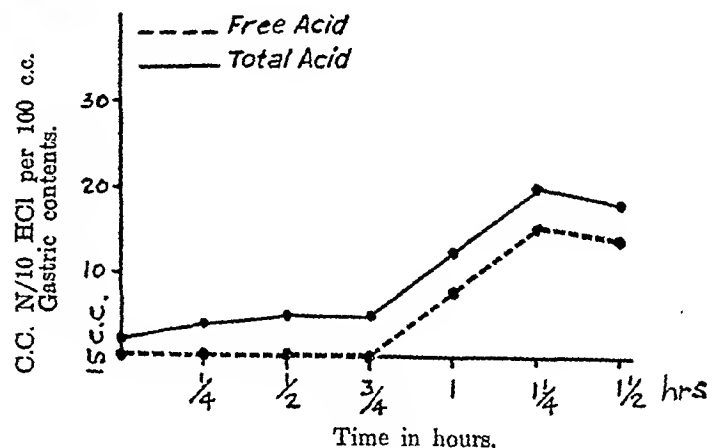


Fig. 7.—Post-operative curve. 11-9-42.

from the area of the general peritoneal cavity surrounding the cyst, so as to drain away any fluid that leaked through.

The patient made an uneventful recovery, and was discharged on 30th July, 1942. Since operation, the condition of the patient has remained excellent. He has had no pain whatever, has a good appetite, and has put on 17 lb. in weight

in 6 months. There is no evidence so far of any recurrence of the swelling, and he is back at his work. The condition of the stomach after operation is shown in the barium-meal skiagrams (plate XIV, figures 3 and 4), where the filling defect is now completely absent and the stomach appears normal. Fractional test meal curves before and after operation are also appended (see figures 5, 6, and 7) and these show that the operation has not seriously affected the condition of the stomach.

Discussion

Jurasz's two cases (Jurasz, 1931) are possibly among the earliest to be recorded of primary anastomosis of the cyst to the stomach. He did this by incising the anterior stomach wall and passing the cautery through the posterior stomach wall directly into the cyst. The fistula thus made was left draining permanently into the stomach (Rowlands and Turner, 1936). Anastomosis of the cyst to the jejunum or the gall-bladder has been suggested by Karl Meyer for non-perforated cyst (quoted by Koucky *et al.*, 1941). This treatment, primary anastomosis to the stomach (or possibly to the duodenum or jejunum as an alternative), appears applicable to all cases of pancreatic cyst (true and pseudo-cysts included), in which marsupialization has hitherto been the operation of choice. A possible exception may be in the case of hydatid cysts where marsupialization may be the safer procedure.

While it is true that cure fairly often occurs with marsupialization, it has several disadvantages. (1) The period of drainage required before the cyst wall granulates and the space is obliterated is sometimes very long, two years or even more, and there is all the inconvenience of a discharging sinus during this time. Kerr reported a case in which the fistula had drained for 15 years (quoted by Judd *et al.*, *loc. cit.*). (2) The inconvenience of a discharging sinus would not be so serious were it not for the associated troublesome excoriation of the abdominal wall which occurs often enough in spite of all care. To prevent the occurrence of, or to lessen, this excoriation, various local applications such as N/10 HCl, 10 per cent Witte's peptone, and various ointments, diet with excess of carbohydrates and fat, anti-diabetic diet, etc., have been recommended. In persistent cases, applications of radium and deep x-ray therapy have been tried. The discharge may be as much as 20 to 30 ounces or even more in 24 hours, and continuous suction drainage has been employed. The very multiplicity of the methods recommended shows that the disability is real and serious. Even secondary operations such as dissecting up the sinus track and implanting it into the stomach, duodenum, jejunum or gall-bladder have been carried out. Such secondary operations, because of extensive adhesions resulting from the original operation and because of the existence of a long standing sinus, are

likely to be more hazardous than the operation of anastomosis at a single sitting. (3) Sometimes secondary infection of the cyst wall occurs through the drainage track, exposing the patient to the dangers of chronic sepsis and hæmorrhage. The writer has experience of a case in which mild secondary infection occurred, and elaborate arrangements for continuous irrigation and drainage had to be maintained for several weeks before the patient recovered. He became extremely ill and anæmic, and rallied with great difficulty. The literature contains similar cases. In one of these, the discharge became very foul after marsupialization, secondary stones developed in the sinus, and ultimately the patient recovered after the sinus track had been implanted into the jejunum. The patient had been in and out of hospital for nearly three years before ultimate recovery. A study of these case reports suggests that it might have been possible, even in the very first stage, to anastomose the cyst into the bowel. (4) Even if the discharge ceases and the wound heals, recurrence of the cyst is not unknown.

Hitherto very little attention has been paid to this method of treatment by most authorities. The possibility of leakage at the line of anastomosis due to the digestive action of pancreatic juice, with the attendant dangers of pancreatic necrosis or peritonitis, have probably acted as a deterrent factor; or perhaps it is the fear that, if the cyst is drained into the stomach, the pancreatic secretions may act detrimentally on the gastric mucous membrane, or that regurgitation of stomach contents into the pancreatic duct may occur, with the dangers of acute hæmorrhagic pancreatitis. These dangers seem more apparent than real. It is known that equal volumes of pancreatic and gastric juice neutralize each other. Further, neutralization of the acid gastric secretion is effected in health by many factors, but principally by the alkaline pancreatic juice. In normal circumstances there is frequent regurgitation of this fluid through the pylorus into the stomach. Further, the chances of the cyst contents being exclusively of undiluted pancreatic juice are remote. Many true cysts, and the majority of pseudocysts, contain very little pancreatic juice. The greater part of the bulk in pseudocysts is due to the outpouring of a large amount of fluid from surrounding tissues in response to the intense irritation caused by a small quantity of pancreatic juice. Indeed, in some cases of cyst undoubtedly of pancreatic origin, the cyst contents do not contain pancreatic ferments. This may be due to the fact that chronic disease of the gland interferes with its secretory function Turner (Choyce and Beattie, 1923). As for the danger of regurgitation of stomach contents into the pancreatic duct, and of consequent pancreatic necrosis, there is reason to believe that this too is not real. Further, there is often no communication between the cyst wall and the pancreatic duct. Even if it exists, as appeared probable in the case

reported here, the operation was followed by no ill consequences. As already mentioned, Jurasz's two cases, in which he drained the cyst into the stomach, did very well. The success of the method in these few reported cases appears to justify further trial. Referring to implantation of fistulæ tracks resulting from marsupialization, Janes (1934) expressed the opinion that, while the implantation of such tracks into stomach, gall-bladder, duodenum, or jejunum has been done, implantation into the stomach would appear to be preferable because of the safety with which it may be carried out.

Pancreatic cysts are not common, but they do appear occasionally for treatment in large institutions. The writer has seen a few cases operated on, and in retrospect feels that, in all of them, primary anastomosis to the stomach could have been done, though marsupialization was the operation that had been performed.

Points of clinical interest in the present case are the mobility of the cyst and its intermittent disappearance and refilling. It is usually held that pancreatic cysts are not movable, but more than one observer has stated that they may be movable. In this particular case, it was movable in a transverse axis to a certain extent, and markedly movable up and down during respiration. In another case of tumour of the head of the pancreas in the writer's experience (verified by operation), the tumour was extraordinarily movable, and ballottement could be elicited. There was some difficulty in the diagnosis. Since the loin was not filled and the tumour was fairly central, the idea that it might be a tumour of a floating kidney was entertained, but this was excluded by a pyelogram. At operation, it was seen that the tumour arose from the head of the pancreas, had a broad base, and had infiltrated the entire gland. There were secondary enlargements of the glands in the mesentery of the small intestine. No pedicle was found to explain the undue mobility of the tumour.

Attention has already been drawn to the fact that the tumour in the present case ascended in the erect posture. A possible explanation seems to be as follows. In the recumbent posture the coils of intestine are around the swelling. In the erect posture they gravitate below the swelling and the tumour mass 'floats' up. The tumour of the head of the pancreas referred to, also rose to a higher level in the erect posture.

The intermittent filling and disappearance of such cysts have previously been observed. Judd *et al.* (*loc. cit.*) noted two cases in their series, with a history of such disappearance, and cited a case of Payr (1898) in which the tumour disappeared and recurred thrice in two months. In some cases, with the disappearance of the cyst, the patient had an attack of diarrhoea. The patient reported here was ordinarily constipated, but had a lax bowel after the disappearance of the cyst. The disappearance of the cyst may possibly be due to a connection with the

pancreatic duct or some part of the alimentary canal. None however could be located at operation. It seemed unlikely that rupture of the cyst had occurred. The fluid contents of the cyst showed only amylase. There was no trypsin or lipase; such findings, in cases of definite pancreatic cyst, are numerous in the literature (Judd *et al.*, *loc. cit.*).

Anastomosis of cysts to other parts of the intestinal tract may be considered. Anastomosis to the duodenum is likely to be more difficult than to the stomach, but, if possible, is ideal. Anastomosis of a fistula to the gall-bladder has been performed, but seems a poor alternative. Reports of cases of fistulæ anastomosed to the stomach have been the most favourable. The gastric route of approach to cysts deserves an extended trial.

Summary and conclusion

A case of pancreatic cyst anastomosed to the stomach is presented, and the advantages of this method of treatment are discussed.

Acknowledgments

Thanks are due to Major F. A. B. Sheppard, I.M.S., Superintendent, King George Hospital, for permission to publish this case; to Dr. Bhaskara Menon, Professor of Pathology, for valuable suggestions in the preparation of this paper; to Dr. V. K. Narayana Menon, Professor of Biochemistry, for the bio-chemical reports; to Dr. Benjamin, the Radiologist, for the photographs and skiagrams.

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THE TREATMENT OF TÆNIASIS

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(a) Carbon tetrachloride.

A CURE rate of 75 per cent with carbon tetrachloride having been obtained by Maplestone and Mukerji (1931) in 25 cases of *tania* infection, the treatment with the drug was continued and we have now completed the records of 58 cases. In the paper mentioned above, the results of single treatments were shown, those patients who were not cured by one treatment being listed again when subsequent treatments were given. In this paper, we have shown the results of one, two or three treatments as given to the 58 persons including those mentioned in our previous report.

Method of administration.—No preliminary purgative was given. The patients were allowed

Criterion of cure.—If the entire worm with the scolex was passed, and strobila of additional worms were not seen, the case was believed to be cured, but nevertheless some of them were followed up for a period of five months or longer. Those that did not pass the scolex after the treatment were followed up, and if they were free from the segments three months or longer, they were believed to be cured.

Material.—There was only one case of *Tania solium* in this series. All the others had single infections with *Tania saginata* except one, who passed two scolices.

Results of treatment.—The after-histories of 16 patients were not available. Of the remaining 42 who reported to us, 28 were cured by one treatment. Scolices were found in 14 only. Seven of the 14 uncured were given a second treatment and six were cured; scolices were found in 2 only. To the remaining 1 still not cured, a third treatment was given and even then he was not cured (with three doses of 48 minims each).

TABLE I.—Carbon tetrachloride

Dose in minims	ONE DOSE				TWO DOSES		
	Treated	Cured	Not cured	Not traced	Treated	Cured	Not cured
48	38	22	5	11	3	2	1
40	3	2	1	0	1	1	0
32	3	1	0	2
24	4	0	2	2
20	3	0	2	1	1	1	0
16	4	2	2	0	1	1	0
10	1	1	0	0
8	2	0	2	0	1	1	0
	58	28	14	16	7	6	1

a meal of milk and bread the previous evening about 7 p.m. and no food was given afterwards. Early the next morning, before they had any food, the dose of carbon tetrachloride was administered, in 9 cases followed by a dose of salts given one and a one-half to two hours later, and to the rest actually mixed with the dose of salts, either magnesium sulphate or sodium sulphate. No food was allowed until there was satisfactory bowel movement. The dose of salts was repeated in four hours if necessary. All the stools were collected during the next 48 to 72 hours, and a careful search was made for the scolices.

Dose.—The dose varied from 8 minims to a maximum of 48 minims (3 c.cm.) according to age, 38 patients having received the maximum dose. No toxic symptoms were noticed except dizziness and drowsiness in a few, which passed off rapidly.

* This work was done conjointly by the two authors, but the paper was written up by A. K. Mukerji after Dr. Maplestone left India.

All the patients reported as not cured by one treatment did not come for the subsequent treatments. Those who came were of course given a second treatment, but the results of these subsequent treatments could sometimes not be ascertained.

Some of the 16 patients whom we could not trace must have been cured. Leaving them out, however, we found that 34 out of 42 were cured by either one or two treatments with different doses (a cure rate of 80 per cent). With the maximum dose of 3 c.cm. 24 out of 27 were cured, (about 89 per cent).

(b) Tetrachlorethylene

We have treated 106 patients altogether, 53 in our hospital and 53 in the out-patients department, including the 26 cases reported by Maplestone and Mukerji (1937). The method of administration was the same as that used with carbon tetrachloride, and the drug was given shaken up in dose of salts. All the stools of the in-patients were collected for 48 or 72 hours,

and a careful search was made for the scolices. In the case of the out-patients, it was not possible to get them to bring all their stools for examination, but some of them brought all that they passed on the day of treatment. The criterion of cure was the same as that with carbon tetrachloride. The maximum dose given to an adult was 64 minims (4 c.cm.) and proportionately smaller doses to the children or the undernourished individuals.

Results of treatment.—Of the 106 patients treated, 45 failed to report. Thirty of the remaining 61 were cured by one treatment. A second treatment was given to 10 of the 31 uncured, and 3 more were cured. Scolices were found in 4 only. There were two cases of experimentally induced *T. solium* infection in this series; one of these passed four scolices. All the others had *T. saginata* infection, single worms only except one who passed four worms without scolices.

Method of administration.—After a meal of milk and bread at 7 p.m. the previous night, the drug freshly put up in hard gelatine capsules was given early in the morning and no food was allowed for four hours afterwards. No purgative was given on that day. If there was no bowel movement during the day, which happened rarely as the drug itself has laxative properties, a dose of salts was given the next morning.

Dose.—The full dose of one gramme was given to 22 patients; the other 3 received 0.75, 0.5 and 0.4 gm. respectively.

Results of treatment.—Six out of the 25 were not traced. Five of the remaining 19 were cured by one treatment, and 4 more by two treatments; 10 were not cured by one treatment. A scolex was passed in one case only, and the others free from the segments from three months to six months were believed to be cured. Thus there were 9 cures out of 19, about 47 per cent.

TABLE II.—*Tetrachlorethylene*

Dose in minims	ONE DOSE				TWO DOSES		
	Treated	Cured	Not cured	Not traced	Treated	Cured	Not cured
64	76	27	19	30	4	3	1
48	3	1	0	2	1	0	1
40	2	1	1	0	1	0	1
32	9	1	3	5	1	0	1
24	4	0	2	2	1	0	1
20	3	0	2	1	1	0	1
16	4	0	2	2	2	0	2
10	5	0	2	3	1	0	1
	106	30	31	45	10	3	7

TABLE III.—*Hexylresorcinol*

Dose in gm.	ONE DOSE				TWO DOSES		
	Treated	Cured	Not cured	Not traced	Treated	Cured	Not cured
1.0	22	5	12	5	3	3	0
0.75	1	0	1	0	1	1	0
0.5	1	0	1	0	1	1	0
0.4	1	0	0	1	1	1	0
	25	5	14	6	4	4	0

Leaving out the 45 not traced, 33 out of 61 were cured by one or two treatments of different doses, giving a cure rate of 54 per cent. With the maximum dose of 4 c.cm., 30 out of 46 were cured (about 65 per cent), much less than the cure rate with carbon tetrachloride. No toxic symptoms except dizziness were noticed with tetrachlorethylene.

(c) *Hexylresorcinol*

We have treated 25 cases of *T. saginata* infection altogether including the 10 cases reported by Maplestone and Mukerji (1932).

Conclusions

We thus find that carbon tetrachloride is the best drug of the three, giving a cure rate of 80 per cent, as against 54 per cent with tetrachlorethylene and 47 per cent with hexylresorcinol. Carbon tetrachloride may, therefore, be regarded as the treatment of choice in tæniasis, provided there are no contra-indications to its use.

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A NOTE ON GIARDIASIS WITH STEATORRHOEA

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THE significance of *Giardia intestinalis* in the stools has long been controversial. It is a common parasitic intestinal flagellate. Some observers consider that, like other intestinal flagellates, this parasite is also a harmless organism; many healthy persons so infected have no symptoms whatsoever. Others hold that this fact alone cannot be regarded as evidence of its non-pathogenicity, for many apparently healthy individuals harbour, for example, *E. histolytica* but show no symptoms. Some regard it as pathogenic, and as able to cause symptoms such as diarrhoea, vague abdominal discomfort or pain, children being the worst sufferers. The recognition of successful atebirin therapy in giardia infection in recent years has provided a useful means of investigating the pathogenicity of this organism; many observers at present are inclined to take the view that in some patients it is responsible for disorders of the digestive system (Chopra *et al.* 1939).

The duodenum and upper part of the small intestine are the common sites of giardia infestation. It may injure the epithelium and interfere with the function of the small intestine, e.g. absorption of fat. McGrath *et al.* (1940) reported a fatal case of giardial steatorrhoea with organic lesions in the intestine. O'Donovan *et al.* (1942) recorded a case of giardiasis in a boy; the symptoms and findings resembled those of idiopathic steatorrhoea.

In view of these observations, the following account of a case of steatorrhoea associated with *Giardia intestinalis* seems worth reporting:—

A Hindu widow, aged 48 years, was admitted to the Carmichael Hospital for Tropical Diseases on March 23, 1942. The chief complaints were diarrhoea, flatulence, irregular fever, and swelling of the legs.

The patient stated that for the last 10 years she had suffered from dyspepsia, 'acidity', flatulence, and occasional pain in the abdomen. Diarrhoea started seven months ago; at first it was intermittent, alternating with constipation, but lately, it had been persistent, with three to four motions a day, the stools being bulky and pale and without blood or mucus. Flatulence had been very troublesome, especially after meals; at times she felt 'suffocated' due to gaseous distension of the abdomen. The legs began to swell about six months ago, and once she had noticed swelling of the hands and face. The fever was of recent origin. The abdominal pain was griping in character, and occurred mostly while passing stools. The appetite was not good; moreover, she was afraid to eat on account of flatulent distension.

There was nothing particular in her family history and previous history. Being a Hindu widow she was a strict vegetarian.

The patient was thin and rather emaciated, with a slightly protuberant abdomen. The legs were oedematous and shiny. The temperature on admission was 101°F.; pulse 100 and respiration 24 per minute. She weighed 62 pounds. The abdominal wall was very flabby; the liver was palpable and slightly tender. The

spleen was not palpable. She had pyorrhoea. The tongue was clean and not sore. There was no abnormality in the heart. The blood pressure was 90/60 mm. of Hg. She had no cough, and the lungs were clear. She complained of dim vision, possibly due to early cataract. The knee jerks were brisk. The calves were distinctly tender. There were no symptoms of tetany. On admission, the patient ran a low intermittent temperature, and had three to seven motions a day. The stools were white and copious.

Investigation.—The stools were examined consecutively for 4 days. *Giardia intestinalis* cysts were found, each time in fair number, and scanty trophozoites twice. No ova were seen. The stool was cultured 4 times, but no pathogenic bacterium was isolated. Chemical analysis of the fat content of the faeces showed:—

Total fat	29.6 per cent.
Neutral fat	13.3 " "
Fatty acids	9.4 " "
Soap fat	6.9 " "

The urine showed no abnormality except a few pus cells.

The detailed blood findings need not be given here. They indicated a moderate degree of macrocytic anaemia.

Van den Bergh reaction—bilirubin content 0.2 mg. per 100 c.cm. of blood. Erythrocytic sedimentation rate—125 millimetre in one hour (Westergren method). The Wassermann, aldehyde and antimony tests were negative. The glucose tolerance test (oral) and the intravenous glucose tolerance test gave results within normal limits.

Gastric analysis by the fractional method showed achlorhydria with very slight response to histamin.

X-rays after barium meal showed:—*Stomach* hypotonic or J-type. There was no evidence of ulcer or neoplasm. Emptying time normal.

Duodenum.—Nothing definitely abnormal noted; cap normal.

Small intestine.—Nothing abnormal noted. There was no evidence of dilatation, segmentation, or deficiency pattern of the small intestine.

Large intestine.—Some degree of hypermotility.

Treatment.—In view of the pseudo-achlorhydria and macrocytic anaemia, the patient was put on an acid-pepsin mixture and also given a course of liver injections (T.C.F. crude). This helped her flatulence, and lessened the number of stools, but the colour of the stools was not changed.

The blood picture showed general but moderate improvement. Details need not be given here.

The Van den Bergh reaction was negative, and ESR (Westergren) was 95 mm. (one hour). There was a temporary leucocytosis, due to a local inflammation at the site of a liver extract injection.

The patient felt better after the above treatment; she had no more fever. Her weight came

down to 57½ pounds, as her œdema had almost subsided. The character of her stools was still white and greasy.

On account of her giardia infection with steatorrhœa, she was put on crinodora (a substitute for atebrian), 0.1 gramme thrice daily for 5 days, and the acid mixture was continued, the dose of dilute hydrochloric acid being increased to one drachm.

With this treatment, her diarrhœa stopped completely, and the stools became normal in colour. She had no more pain in the abdomen. The stools were again examined for 6 consecutive days; no *Giardia intestinalis* was found.

Subsequently, owing to persistent pain in the legs, she was given a course of vitamin B₁ injections, and her teeth were attended to. This helped her very much, and she could now walk comfortably.

During convalescence she had slight diarrhœa for 2 days; this was readily controlled by a few doses of sodium sulphate mixture.

She was discharged cured on 11th May, when her weight was 67½ pounds.

Summary and conclusions

A case is reported with symptoms suggestive of sprue or 'para-sprue'. Steatorrhœa, macrocytic anæmia, pseudo-achlorhydria and giardiasis were the main findings. The general condition improved with liver therapy and acid mixture, but the steatorrhœa persisted. Eradication of giardia infection coincided with the cessation of steatorrhœa.

It is difficult to estimate the exact rôle played by the *Giardia intestinalis* in causing fatty diarrhœa, but since there was no evidence to account for this condition, it is possible that this infection deranged the function of the small intestinal epithelium interfering with the absorption of fat. The clinical improvement immediately after the specific treatment does suggest fairly strongly that the presence of giardia was more than a fortuitous association.

Acknowledgment

I should like to express my grateful thanks to Dr. L. E. Napier, for his frequent advice on the investigation and treatment of this patient and for his kind permission to report the case. My thanks are also due to Dr. J. P. Bose who carried out the biochemical investigations.

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THE SEARCH FOR AN ANTI-MALARIAL DRUG IN THE INDIGENOUS MATERIA MEDICA

PART II—*Casalpinia bonducella*, Fleming

By B. MUKERJI

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and

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Introduction

Casalpinia bonducella (N. O. Leguminosæ), commonly known as 'bonduc nut' or 'fever nut' in English, as 'nata' or 'natakranja' in Bengali, and as 'katkaranj' in Hindi, has long been known to the Hindu and Mohammedan physicians for its medicinal properties. The root, bark, leaves and the seeds have all been used in indigenous medicine, but the seeds or their yellowish-white kernels are generally considered as possessing well-marked anti-periodic properties, and are largely used by practitioners of indigenous systems of medicine in acute and chronic fevers as a substitute for quinine. For this purpose, the seeds or seed kernels are pounded with black pepper, and a dose varying from 5 to 30 grains is administered by mouth. In 1868, the seeds were made official in the Pharmacopœia of India, a dose of 15 to 30 grains of the powdered seeds being recommended as a safe anti-pyretic, and their use was favourably reported upon by several medical officers. An investigation of the anti-malarial properties of these nuts was therefore undertaken with a view to finding out if there is any action in experimental and clinical malaria.

Chemistry, pharmacology, etc.

Heckel and Schlagdenhauffen (1886) first attempted to isolate the constituents of *Casalpinia bonducella* nuts. They obtained a non-alkaloidal bitter principle from the kernel, in the form of a white powder (bonducin) to which they gave the formula C₁₄H₁₆O₆; they attributed the physiological properties of the seeds to this constituent. Bacon (1906) isolated the bitter principle 'bonducin' from the seed kernel, and gave evidence to suggest that it was a mixture of complex resinous bodies. He failed to detect any glucoside or alkaloid in the alcoholic extract of the kernels. Bhaduri (1912) claimed to have separated an alkaloid from the kernel, and suggested the name 'natin' for it, but no details were given in support of his findings.

Godbole, Paranjpe and Shrikhande (1929) isolated the bitter principle from the alcoholic extract of the kernel, and concluded that it was a sulphur-containing glucoside. Chopra, Ghosh and Dutta (1929) attempted to separate the active principle from the seeds, but found, on careful examination, the presence of only a bitter principle of non-glucoside nature, insoluble in

water but soluble in alcohol. The presence of an alkaloid as reported by Bhaduri could not be confirmed. Katti (1930) isolated a bitter principle of a complex resinous character in the petroleum ether extract. Ghatak (1934) reported the presence of a non-crystalline bitter glucoside (bonduein) in the kernel of the seeds, having a molecular formula $C_{20}H_{28}O_8$, and being insoluble in water but soluble in alcohol, acetone, pyridine, chloroform and carbon tetrachloride.

Chopra *et al.* (*loc. cit.*) studied the pharmacological action of the non-glucoside bitter principle, but found it to be devoid of any activity, as far as general pharmacological tests were concerned.

Experimental

(a) *Alcoholic extract of C. bonducella.*—As the present work was primarily designed for the evaluation of the anti-malarial property of the drug, no attempt was made to work out in detail the complicated chemistry or to isolate the individual components of the seeds. Previous experience appeared to indicate that an alcoholic extract of the seed kernels freed from fat would contain all the active principles likely to possess anti-malarial properties. For experimental trials, an alcoholic extract was, therefore, prepared in the following manner.

Two hundred grams of the dried powdered kernel (constituting about 45 per cent of the entire seeds) were extracted with petroleum ether in a small percolator. The residue was taken out, dried in air and more finely powdered, and again extracted with petroleum ether (B.P. 40° to 60° cg.) until it was free from fatty matter. The petroleum ether extract, on evaporation, left a greenish yellow thick oil with a disagreeable odour. The oil gave no reaction for alkaloids or glucosides. Finally, the powdered drug was extracted with rectified spirit in a Soxhlet apparatus until completely exhausted. The alcoholic extract, on evaporation in vacuum, left a residue which was found to be very bitter in taste, but it gave no reaction for the presence of alkaloids. The yield was found to be approximately 15 per cent.

(b) *Pharmacological studies.*—Detailed pharmacological investigations of the alcoholic extract could not be undertaken, as a soluble preparation of the active principle suitable for parenteral injection could not be obtained. The toxicity, when administered by the oral route, of the alcoholic extract (trituated with 2 c.cm. water to form an emulsion) was however roughly determined on cats and rabbits. The toxicity was found to be on the low side, as a dose of nearly 1 gm. of the extract (after evaporation of alcohol) per kilo body-weight was well tolerated in both these animals. This dose being much higher than the therapeutic dose recommended of the bonducella nut powder (15 to 30 grs. for a person weighing 60 kilo body-weight), it was not considered worth while for purposes of this investigation to determine accurately the toxicity of the alcoholic extract. All animal experiments

were conducted with a dose larger than the recommended therapeutic dose, but smaller than 1 gm./kg. body-weight of the alcoholic extract.

(c) *Chemotherapeutic studies.*—Unlike the study reported previously by the authors (1942) on monkey malaria with the total alkaloids of *Alstonia scholaris*, this investigation was carried out with fowl malaria. The difficulty in feeding monkeys with a definite dose of the alcoholic extract through a stomach tube could not be easily overcome, and it was not possible to prepare an injectable preparation of the active principles. Domestic fowls, on the other hand, could be comparatively easily handled, and the drug was given in small quantities by mouth, care being taken to see that no regurgitation took place.

Fowl malaria experiments were chiefly conducted by one of us (L. B. S.). Domestic fowls, weighing on an average from 350 to 400 gm., were inoculated either intravenously or intramuscularly with $\frac{1}{2}$ c.cm. of citrated blood from fowls showing a normal infection with the strain of *P. gallinaceum*, Br., originally isolated from a jungle fowl by Brigadier H. E. Shortt, I.M.S., in Madras. The experimental fowls were treated with the alcoholic extract of *C. bonducella* after parasites had been observed in the peripheral blood. The drug was administered by the oral route in daily doses of 2 c.cm. of a 5 per cent (100 mg./2 c.cm.), 10 per cent (200 mg./2 c.cm.) and 20 per cent (400 mg./2 c.cm.) emulsion. Control birds were treated with intramuscular injections of mepacrine hydrochloride (synthesized in Calcutta by two local firms) in a dosage of $\frac{1}{2}$ to 1 mg. per 20 gm. of body-weight dissolved in $\frac{1}{2}$ c.cm. of distilled water. The anti-malarial properties of the drugs were judged by their effects on the infection rate of the blood cells from day to day, and on the morphology of the parasites. The number of infected cells was counted in totals of 1,000, 500 or 100 red blood cells, according to whether parasites were very scanty, readily observed or extremely numerous. A negative result was recorded only when parasites could not be detected in a thin film after a full three-minute search.

The results of the experiments are represented in three columns in tabular form (*see table*).

In the first experiment, two fowls (nos. 400 and 404) were treated with three daily doses each of a 5 per cent and a 10 per cent emulsion of bonducella extract respectively, while a third control fowl (no. 402) was left untreated. In all three birds, the progressive increase in the numbers of parasites was manifest in the rising infection rate of the red cells, the highest values in the case of treated birds being recorded after treatment with three doses. The comparatively low peaks of infection of 8 to 26 per cent were undoubtedly due to the early death of both treated and untreated birds from an unknown cause. No evidence of degeneration of the parasites was obtained in the treated birds.

TABLE

Showing lack of action of alcoholic extract of *C. bonducella* ('Nata') in fowl malaria *P. gallinaceum*, Br.)

Expt.	TREATED FOWLS					UNTREATED CONTROL FOWLS			REMARKS
	Bird number	Treatment	Percentage infection of r.b.c.			Bird number	Percentage infection of r.b.c.		
			Before treatment	After treatment	Peak		First positive examination	Peak	
I	400 404	Three doses 'nata' 5%. Three doses 'nata' 10%.	Less than 0.1 1.4	8 22	8 22	402	Less than 0.1	26	All three birds died early. Cause of death doubtful.
II	440	(i) Three doses 'nata' 10%. (ii) Further treated with 3 doses (10 mg. each) of mepacrine hydrochloride.	0.6 80	80 1	80 ..	439	0.2	55	No. 439 was later treated with 3 doses of mepacrine hydrochloride; infection fell to 2 per cent. In both birds, degeneration of parasites observed after treatment with mepacrine hydrochloride.*
III	442 443 (control).	Six doses 'nata' 20%. Three doses of 10 mg. of mepacrine hydrochloride.	1 4	22 1	80 4	441	1.4	87	No. 443 became negative 2 days after the last dose of mepacrine hydrochloride.†

* Both birds died later showing infection of endothelial cells of the brain capillaries.

† All three birds died showing infection of the endothelial cells of brain capillaries.

In the second experiment, another fowl (no. 440) was treated with three doses of a 10 per cent solution of *C. bonducella* extract. A control bird (no. 439) was kept untreated for a period of five days, during which time the infection rate had risen to 55 per cent. In fowl no. 440, the infection rate rose from 0.6 per cent to 80 per cent in the three days during which the drug was given. The parasites were normal in every way. Both birds were then treated with mepacrine hydrochloride and an immediate response was observed in the form of degenerating parasites. The infection rates dropped precipitously to 1 per cent in fowl no. 440, and 2 per cent in fowl no. 439. The birds died seventeen to twenty-one days after the inoculation, showing infection of the endothelial cells of the brain capillaries with the remarkable exo-erythrocytic forms which are known to be resistant to anti-malarial drugs.

In the final experiment, one fowl (no. 442) was treated with six doses of 20 per cent solution of *C. bonducella* extract, while of two controls, one was treated with mepacrine hydrochloride (0.5 mg. per 20 gm. approximately of body-weight) and the other not treated. The infec-

tion rate in no. 442 rose from 1 to 22 per cent during the six days' treatment, and two days later reached the quite normal figure of 80 per cent. The untreated bird (no. 441) showed similar findings. The bird treated with mepacrine hydrochloride never showed an infection rate higher than that seen before treatment, namely 4 per cent, although it lived for nineteen days after inoculation. Degenerating parasites were observed in this bird. All three birds died showing exo-erythrocytic schizonts in the brain capillaries.

(d) *Clinical studies.*—The wide popularity and reputation of the so-called 'fever nuts' led the Indigenous Drugs Committee of Madras (1924) to give clinical trials of the seed powder in several hospitals (Chopra, 1933). Though the recorded findings do not definitely justify the conclusions arrived at (there being no data of regular blood examinations and demonstration of parasites in cases diagnosed as malaria), the Committee recommended the use of the drug as a valuable anti-periodic, febrifuge and effective tonic.

(Concluded on next page)

LETHAL ACTION OF POTASSIUM PERMANGANATE ON VIBRIOS

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Potassium permanganate pills were used by Rogers (1913) in cholera cases to neutralize the toxins of the cholera vibrio, and permanganate is commonly used to disinfect clothes, well water and tank water, cholera stools, etc., during an epidemic. Hands also are often washed with permanganate solutions after attending cholera

(Continued from previous page)

Due to the paucity in Calcutta of definitely proved malaria cases untreated with other anti-malarial drugs during the winter months, our attempts to give the alcoholic extract of *C. bonducella* a thorough clinical trial were not successful. However, its administration in one proved case was far from encouraging. Further clinical trials might be undertaken during the malaria season but are perhaps not justifiable.

Summary and conclusions

An alcoholic extract of *C. bonducella* nuts (fat-free powder prepared from the kernels) when fed in a dose up to 400 mg. per gm. body-weight failed to arrest the normal multiplication of *P. gallinaceum* in domestic fowls; moreover the parasite showed no change in morphology. Mepacrine hydrochloride (atebrin) synthesized by local manufactures in Calcutta produced both these effects. These results do not encourage tests with 'nata' on other malarial infections—animal or human. It appears unlikely that 'nata' has any specific action in malaria.

Acknowledgment

Thanks are due to Dr. B. M. Das Gupta, Director, and to Dr. S. Ghosh, Professor of Chemistry, School of Tropical Medicine, Calcutta, for placing the facilities of their laboratories at the disposal of the workers.

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cases. There are various old references to potassium permanganate in dilutions as high as 1 in 500,000 being lethal to the cholera vibrio, but not to other organisms, and therefore the matter needs reinvestigation in the light of our present knowledge.

In the present paper are reported the results of a study of the effect of various dilutions of potassium permanganate on the cholera vibrio and on some other organisms. Standard numbers of organisms were treated for varying times with potassium permanganate in varying dilutions.

Permanganate is well known as an oxidizing agent of organic matter. The chemical is weakened and its colour is discharged in the presence of an excess of organic matter. Hence to demonstrate the full effect of the drug, extraneous organic matter was excluded as far as possible by washing the vibrios three times in normal saline.

The deposit present after centrifugation of the permanganate-treated suspension was again suspended in saline, and the number of vibrios was estimated by matching with opacity tubes. These procedures were carried out within the shortest time possible.

Recently isolated virulent strains were used in the experiments. The dilutions of potassium permanganate were made in sterile flasks containing 100 c.cm. of sterilized pyrogen-free, redistilled water at pH 6.8. The required number of vibrios in a small quantity of inoculum was then added to the solutions, and the suspension was well shaken and kept at room temperature. Subcultures were made at specified intervals with 0.5 c.cm. spread on nutrient agar, and, if no growth was seen in 24 hours, 1 c.cm. of the suspension, after vigorous shaking, was seeded into 10 c.cm. of peptone water to confirm its sterility. A control test was put up without the addition of permanganate. It was found that the discharge of pink colour was not necessarily an indication of multiplication and growth of vibrios. In high dilutions of the permanganate, the colour was barely visible, but still the solution showed bactericidal properties. After mixing and incubation, the colour was discharged in some, but vibrios were still found killed.

The following tables show the results of the experiments.

It will be seen from the tables below that potassium permanganate in a high dilution such as 1 in 10^6 with hardly any visible colour, exerts a bactericidal effect on Inaba and Ogawa subtypes of *Vibrio cholerae* in $\frac{1}{2}$ to 20 hours. A still higher dilution of 1 in 10^9 kills the non-agglutinating vibrios. In contrast to its lethal action on *V. cholerae*, potassium permanganate in a much higher concentration fails to kill even a smaller number of *Bact. typhosum*.

As vibrios are generally present in nature in association with organic matter, it was felt necessary to see how the organisms would react to permanganate in the presence of organic matter. Washed vibrios were suspended in

TABLE I

Number, of <i>V. cholerae</i> Ogawa sub-type.		CONCENTRATION OF $KMnO_4$ IN 100 C.CM. OF DISTILLED WATER										Control without permanganate	
		1/500		1/1,000		1/5,000		1/10,000		1/50,000			
		Time of contact in hours. Room temperature											
		$\frac{1}{2}$	2	$\frac{1}{2}$	2	$\frac{1}{2}$	2	$\frac{1}{2}$	2	$\frac{1}{2}$	2	$\frac{1}{2}$	2
700×10^6	..	—	—	—	—	—	—	—	—	—	—	+	—
$1,400 \times 10^6$..	—	—	—	—	—	—	—	—	—	—	+	—
$3,500 \times 10^6$..	—	—	—	—	—	—	—	—	—	—	+	+
$7,000 \times 10^6$..	—	—	—	—	—	—	—	—	—	—	+	+
$28,000 \times 10^6$..	—	—	—	—	—	—	—	—	—	—	+	+

Colour of permanganate not completely discharged in any flasks. 0.5 c.c. smeared on nutrient agar slope to test survival.

+ = growth; — = no growth.

TABLE II

Number of <i>V. cholerae</i> Ogawa sub- type.	CONCENTRATION OF KMNO ₄ IN DISTILLED WATER										Control without permanganate			
	1/60,000		1/80,000		1/100,000		1/200,000		1/500,000			1/10 ⁶		
	Time of contact in hours. Room temperature													
	1/2	2	1/2	2	1/2	2	1/2	2	1/2	2	1/2	2	1/2	2
28,000 × 10 ⁶ .. <i>Bact. typhosum</i> 16,000 × 10 ⁶ .	— +	— —	— +	— —	— +	— +	— +	— +	— +	— +	— +	— +	+	+

These dilutions were practically colourless.

TABLE III

Nature and number of vibrios.	CONCENTRATION OF $KMnO_4$ IN DISTILLED WATER							Controlling distilled water alone.
	1/500,000	1/10 ⁶	1/2 × 10 ⁶	1/100 × 10 ⁶	1/200 × 10 ⁶	1/500 × 10 ⁶	1/1,000 × 10 ⁶	
	Time of contact 18-20 hours. Room temperature.							
<i>V. cholerae</i> Inaba sub- type No. 298A 28,000 × 10 ⁶ .	—	—	+	+	+	+	+	+
Ogawa sub- type No. 292A 28,000 × 10 ⁶ .	—	—	+	+	+	+	+	+
Non-agglutinat- ing para- cholera vibrios 28,000 × 10 ⁶ .	—	—	—	—	—	—	—	+

serum broth, and measured quantities of the suspension were added to 100 c.cm. of the permanganate solutions in flasks. The table below shows the results of the experiments. It will be seen that stronger solutions of the chemical are necessary to destroy the vibrios, as some of the

permanganate is utilized in oxidizing the organic matter present in serum broth. As a rule, such an enormous amount of organic matter is not present in natural and artificial waters, and hence it is probable that a much higher dilution of the drug is capable of killing the vibrios

present in such waters. It is also important to note that for complete sterilization, not only the strength of potassium permanganate, but also the number of vibrios in a sample, is to be taken into account; the higher the number of vibrios present, the greater is the concentration of permanganate needed for complete disinfection. For example, when 0.2 to 1.0 c.cm. of a culture of *V. cholera* is added to 100 c.cm. of 1/500 dilution of permanganate, complete sterilization occurs, but when 4.0 c.cm. of the same culture is added, no such action is seen.

of *V. cholera*, in 2 to 20 hours in a dilution of 1 in 100,000, but not in a dilution of 1 in 500,000.

For all these experiments, it is of the utmost importance that the distilled water should be absolutely free from chlorine, which is highly bactericidal to vibrios. Four drops of electrolytic chlorine added to 2 litres of tank water containing 140,000 millions of *V. cholera* killed all the vibrios in the water in half an hour. It is planned therefore to study the action of chlorine and hypochlorites on vibrios.

TABLE IV

Organisms suspended in serum broth.	CONCENTRATION OF KMnO_4 IN DISTILLED WATER														
	1/5,000			1/10,000			1/50,000			1/100,000			Control		
	Time of contact in hours														
<i>V. cholerae</i> Ogawa sub- type $16,000 \times 10^6$.	$\frac{1}{2}$ —	2 —	20 +	$\frac{1}{2}$ +	2 +	20 +	$\frac{1}{2}$ +	2 +	20 +	$\frac{1}{2}$ +	2 +	20 +	$\frac{1}{2}$ +	2 +	20 +

It is seen in the above table that survival of vibrios is shown after twenty hours but not after $\frac{1}{2}$ to 2 hours in a dilution of 1 in 5,000. This appears to be paradoxical. It can be explained by the fact that the majority of organisms were killed in $\frac{1}{2}$ to 2 hours, and the few organisms that survived were not detected by the methods used, but later multiplied in the weaker permanganate solution.

It is also seen from table I that distilled water itself exerts some bactericidal effect, and this is evident only when a smaller number of vibrios is taken for experiment. Hence, in all the above experiments, the effect of the permanganate solution in distilled water was accentuated to some extent by the distilled water. This double effect was not seen when the solution of the drug was made in normal saline.

Experiments were also put up with clean tank water, and the results are given below (table V). It will be seen that permanganate exerts a complete bactericidal effect on a thick suspension

It is also interesting to note that, after the addition of the permanganate, the vibrios are mostly lysed, and the fluid clears, with the formation of a slight brownish deposit at the bottom. Such a preparation lysed with 1 in 5,000 dilution of permanganate was used as a cholera vaccine for inducing agglutinogenic response in rabbits, and for protection tests in guinea-pigs, and the result was the same as that obtained with standard cholera vaccines issued by the Central Research Institute, Kasauli.

Bactericidal action of permanganate on artificially contaminated fruits.—Fruits, such as grapes, apples, bananas, etc., were heavily contaminated with young broth cultures of *V. cholera* and then steeped in permanganate solutions of 1/5,000 and 1/10,000 dilutions contained in clean buckets at room temperature. After 5 minutes, 15 minutes, $\frac{1}{2}$ hour and one hour, cultures were put up at 37°C . with loopfuls taken directly on bile-salt agar plates and also

(Concluded on opposite page)

TABLE V

CONCENTRATION OF KMnO_4 IN 2 LITRES OF TANK WATER. ROOM TEMPERATURE, pH OF WATER 8.3									
Organisms suspended in serum broth.	1/100,000			1/500,000					
	Time of contact in hours						Control without KMnO_4		
	$\frac{1}{2}$ +	2 —	20 —	$\frac{1}{2}$ +	2 +	20 +	$\frac{1}{2}$ +	2 +	20 +
<i>V. cholerae</i> Inaba sub-type $140,000 \times 10^6$.									

STUDIES ON THE ACTION OF DIFFERENT BRANDS OF ATEBRIN IN HUMAN AND SIMIAN MALARIA

By B. M. DAS GUPTA

and

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(a) *Mepacrine hydrochloride* (Bengal Chemical and Pharmaceutical Works, Ltd., Calcutta) in human malaria

THE results obtained in the treatment of simian malaria (*Plasmodium knowlesi*) with Indian mepacrine hydrochloride (Das Gupta and Siddons, 1943) justified tests with this drug in human malaria; these tests are reported in this communication.

Methods

Some typical cases of human malaria in the out-patient department of the School were treated with Indian mepacrine hydrochloride. The dosage in all cases except one was 0.1 gm.

(Continued from previous page)

with 1 c.cm. into 100 c.cm. of alkaline peptone water. The vibrios, however numerous they were before treatment, were all killed in 5 minutes, but in the control buckets without the permanganate, the vibrios were found alive. It is concluded therefore that fruits treated with permanganate solution can safely be eaten.

The same experiments were repeated with *Bact. typhosum* and *Bact. flexneri*, and the organisms were all found to be killed in 5 minutes in a solution of 1/5,000 to 1/10,000.

Summary

Potassium permanganate in a high dilution of 1 in 10⁶ in re-distilled pyrogen-free water is bactericidal to *Vibrio cholerae* and a still higher dilution of 1 in 10⁹ is lethal to non-agglutinating vibrios. Much higher concentrations fail to kill even a smaller number of *Bact. typhosum*. In the presence of organic matter, a lower dilution such as 1 in 5,000 is necessary to kill the vibrios. The destruction of vibrios is associated with their lysis, especially in stronger solution of the drug. A live suspension of cholera vibrios killed with potassium permanganate (1 in 5,000) can be used as a cholera vaccine for producing agglutinating and protective antibodies in animal.

Fruits and vegetables artificially infected with cultures of *V. cholerae*, *Bact. typhosum* and *Bact. flexneri* can be effectively disinfected by soaking them in permanganate solutions of 1/5,000 to 1/10,000 dilutions for 5 minutes.

REFERENCE

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three times daily for five days; in the remaining case (in a boy of 12 years) a dosage of 0.05 gm. for the same period was tried. The drug was given orally in drinking water, one of the daily doses being taken just after the daily blood examination, and the other two at home. Blood films, both thick and thin, were taken immediately before the commencement of treatment, daily during the period of treatment, and for a few days after completion of the treatment. Parasites were counted in the thick films against 100, 500, or 1,000 leucocytes, depending on whether they were readily observed, few in number, or very scanty, and their number estimated per 5,000 leucocytes. A negative result is based on a fairly thorough examination of a thick film about a half-inch square. After completing the course of treatment, the patients were asked to attend at intervals of not more than a week unless they had fever, when they were to come as soon as possible.

Case 1.—A. C. M., a male Bengali, aged 22 years, showed an infection with *Plasmodium vivax*. The effect on the number of the parasites is shown in table I.

TABLE I—*P. vivax*

Date	Number of parasites per 5,000 leucocytes	REMARKS
5-10-1942	6,200	Before treatment, all stages except schizonts were present. Temperature 102°F. at examination.
6-10-1942	350	After three doses, schizonts as well as other forms were present. Temperature 104°F.
7-10-1942	50	After six doses, very scanty parasites were present. Evidence of degeneration of parasites. Temperature 99°F.
8-10-1942	0	After nine doses, thick film negative. Temperature normal.
9-10-1942	0	Negative.
10-10-1942	0	"

The reduction in the number of the parasites after treatment with the drug is striking. Evidence of degeneration was observed, in the form of badly stained parasites of abnormal morphology. The patient did not attend after 10th October, 1942.

Case 2.—T. R., a male Anglo-Indian, aged 40 years, suffering from an infection with *P. falciparum* and showed abundant rings. The results of the daily blood examination are indicated in table II.

As rings did not persist after nine doses (three days' treatment), and the parasites showed degenerative changes, it is assumed that the drug had an inhibitory effect on the asexual cycle.

TABLE II—*P. falciparum*

Date	Number of parasites per 5,000 leucocytes	REMARKS
8-10-1942	23,000	Before treatment, many ring forms and scanty crescents were present.
9-10-1942	15,500	After three doses, degenerate young trophozoites were observed.
10-10-1942	250	After six doses, crescents were chiefly found: in some the pigment was deficient, and in others the pigment showed atypical clumping.
11-10-1942	700	After nine doses, only crescents were present.
12-10-1942	4,000	Crescents only.
13-10-1942	7,000	" "

Case 3.—W. G., a male Anglo-Indian, aged 14 years, showed rings, growing trophozoites and gametocytes of *P. vivax* before treatment. The data from this case are given in table III.

TABLE III—*P. vivax*

Date	Number of parasites per 5,000 leucocytes	REMARKS
1-3-1943	2,700	
2-3-1943	1,050	After three doses, very scanty schizonts were present.
3-3-1943	550	After six doses, about 50 per cent of the parasites were gametocytes.
4-3-1943	200	After nine doses, parasites showed evidence of degeneration.
5-3-1943	90	
6-3-1943	10	Only a trophozoite and a gametocyte were found in a thick film.
9-3-1943	0	Thick film negative.
11-3-1943	0	" " "

After three days' treatment, degeneration of the parasites became evident; they stained badly, so that it was difficult to classify them. A very few persisted after the full course of treatment; these were only observed in a thick film. A few days later, the peripheral blood was found free from parasites.

Case 4.—N. C. D., a Bengali male, aged 12 years, was treated for malignant tertian malaria. A dosage of 0.05 gm. of the drug was tried. Data for this case are given in table IV.

TABLE IV—*P. falciparum*

Date	Number of parasites per 5,000 leucocytes	REMARKS
2-3-1943	2,600	Before treatment, rings and crescents were present.
3-3-1943	1,000	
4-3-1943	200	After six doses, a few rings were still present.
5-3-1943	150	After nine doses, only crescents were observed.
6-3-1943	100	Only crescents present.
7-3-1943	100	" " "
8-3-1943	45	" " "
13-3-1943	20	" " "

As rings disappeared after three days' treatment, and as the patient did not report any further fever, it is considered that schizogony has been suppressed. No clear evidence of degeneration of the parasites was obtained.

Case 5.—S. B., a female Bengali, aged 16 years, showed rings and scanty crescents of *P. falciparum* before treatment. The effect of the drug on the infection is shown in table V.

TABLE V—*P. falciparum*

Date	Number of parasites per 5,000 leucocytes	REMARKS
8-3-1943	14,200	Before treatment, 1.4 per cent of the parasites were crescents.
9-3-1943	11,200	
10-3-1943	240	After six doses, 12.5 per cent of the parasites were crescents.
11-3-1943	140	After nine doses, only crescents were present.
12-3-1943	45	Only crescents were present.
14-3-1943	35	" " " "
18-3-1943	30	" " " "
25-3-1943	10	" " " "

Rings disappeared after three days' treatment and have not been observed since, the last examination being made fourteen days later. Within that period, the patient did not report any fever.

Case 6.—F. K. B., a male Bengali, aged 20 years, showed asexual and sexual form of *P. malariae*. The effect of treatment on the parasites is shown in table VI.

TABLE VI—*P. malariae*

Date	Number of parasites per 5,000 leucocytes	REMARKS
20-3-1943	360	
21-3-1943	300	
22-3-1943	70	After six doses, degenerate parasites were observed.
23-3-1943	50	Degenerate parasites present.
24-3-1943	20	" " "
25-3-1943	15	" " "
26-3-1943	15	An apparently normal gametocyte was seen in a thin film.
30-3-1943	?	A badly stained gametocyte was seen in a thin film.
31-3-1943	0	Thick film negative.

This case of *P. malariae* infection appears to have responded to the treatment, judged from the daily fall in parasite count. However, a few parasites, chiefly gametocytes, persisted up to six days after treatment. Some evidence of the action of the drug was given by the presence of badly stained parasites, the identity of which was sometimes doubtful.

Case 7.—M. Z., a male Bengali, aged 42 years, showed an infection with *P. malariae*, and had a rigor during the clinical examination. Parasitological observations on the case are given in table VII.

TABLE VII—*P. malariae*

Date	Number of parasites per 5,000 leucocytes	REMARKS
26-3-1943	1,250	Temperature was 102°F. just before the first dose.
27-3-1943	450	After three doses, degenerating parasites were observed. Temperature 100°F. just before the fourth dose.
28-3-1943	210	
29-3-1943	30	Degenerate parasites present.
30-3-1943	30	Badly stained gametocyte seen in a thin film.
31-3-1943	10	
3-4-1943	Less than 5	One gametocyte seen in a thick film.
5-4-1943	0	Thick film negative.

In this case, the number of parasites decreased almost daily during treatment, and evidence of direct action on the parasites was obtained. Scanty parasites, chiefly gametocytes, persisted after treatment, and some of these showed degenerative changes.

Summary of results

Seven cases of human malaria (3 of *P. falciparum*, 2 of *P. vivax* and 2 of *P. malariae*) have been treated with Indian mepacrine hydrochloride. It was found that all forms of *P. vivax* disappeared from the peripheral blood in three to five days after the commencement of treatment. After three days' treatment, ring forms of *P. falciparum* were not observed again. Some action of the drug on the sexual forms (crescents) was also apparent. In the *P. malariae* infections, the parasites were much reduced by treatment, but a few forms, chiefly gametocytes, persisted for about a week after the completion of the course of treatment.

(b) *Atabrine* (Winthrop Chemical Co.) in simian malaria

For the tests on simian malaria, the same general methods were followed as in the previous work (Das Gupta and Siddons, *loc. cit.*). In the tests with mepacrine hydrochloride, the infections invariably relapsed after treatment consisting of two or three daily doses of 0.025 gm. It occurred to the authors that longer treatment with smaller doses might be more effective in preventing relapses. Accordingly, some of the tests with atabrine (Winthrop) were carried out in this manner.

Experiment no. 1.—Monkey no. 9, weighing 3½ kilos, showed *P. knowlesi* after an incubation period of six days. It was treated from the second day of the patent period. The protocols of the experiment from the date of treatment are shown in table VIII.

TABLE VIII—The course of infection in monkey no. 9

Date	Infection rate of r.b.c. (per cent)	Treatment	REMARKS
6-1-1943	0.4	0.025 gm.	
7-1-1943	0.4	0.025 "	Degenerate parasites observed.
8-1-1943	0.0	0.025 "	
9-1-1943			
to			
14-1-1943	0.0		
19-1-1943	1.8		Normal parasites.
20-1-1943	2.0	0.0125 "	
21-1-1943	0.4	0.0125 "	Degenerate parasites observed.
22-1-1943			
to			
25-1-1943	0.0		Very scanty parasites.
30-1-1943			
1-2-1943	5.8	0.0125 "	
2-2-1943	2.2		Degenerate parasites observed.
6-2-1943	0.0		
11-2-1943			
to			
29-2-1943	0.0 to 0.6		

Monkey no. 9 has survived *P. knowlesi* infection as a result of treatment with this drug. It is now showing a chronic infection with the parasite.

Experiment no. 2.—Monkey no. 10, weighing 3½ kilos, showed infection with *P. knowlesi* after an incubation period of five days. It was treated from the third day of the patent period. The subsequent course of the infection is shown in table IX.

TABLE IX—*The course of infection in monkey no. 10*

Date	Infection rate of r.b.c. (per cent)	Treatment	REMARKS
13-1-1943	7.2	0.025 gm.	Parasites degenerating.
14-1-1943	4.0	0.025 "	
15-1-1943	0.0	0.025 "	
16-1-1943			
to			
22-1-1943	0.0		
25-1-1943	2.6	0.0125 "	Parasites degenerating.
26-1-1943	1.1	0.0125 "	
27-1-1943			
to			
30-1-1943	0.0	0.0125 "	Four daily doses.
31-1-1943			
to			
6-2-1943	0.0	Stopped	
8-2-1943	Less than 0.1		
11-2-1943	11.0		
12-2-1943	3.2		
13-2-1943	3.2		
15-2-1943	5.0		
16-2-1943	6.0		
17-2-1943			
to			
12-3-1943	0.8 to 0.2		Counts varied within these limits.
16-3-1943	0.0		
29-3-1943	0.6		

This monkey no. 10 has survived a normal infection with *P. knowlesi* as a result of treatment with atabrine.

An indication that a relapse may not require treatment was obtained in this case, as evidenced by the fact that there was a spontaneous decrease in the number of parasites.

Experiment no. 3.—Monkey no. 14, weighing 3 kilos, was found positive for *P. knowlesi* seven days after inoculation. It was treated when the infection rate of the red cells was 20 per cent. Details are shown in table X.

The results in this experiment are very similar to those obtained in experiment no. 3.

Experiment no. 4.—Monkey no. 15, weighing 2½ kilos, showed parasites six days after inoculation. It received a single dose of 0.0125 gm. on 9th February, 1943, when the infection rate of the red cells was 20.4 per cent. The infection rate dropped to 1.8 per cent on 12th February, 1943, and then rose to a secondary peak of 6 per cent on 15th February, 1943. After this date, the infection rate again fell and a chronic infection appeared to have developed, the infection rate varying between 0 and 0.6 per cent.

The monkey is still alive. Evidently a single small dose may be sufficient to save an animal during the primary infection and lead to a chronic infection.

TABLE X—*The course of infection in monkey no. 14 treated with six small doses*

Date	Infection rate of r.b.c. (per cent)	Treatment	REMARKS
7-2-1943	20.0	0.0125 gm.	Mostly degenerating parasites. Very scanty degenerating parasites.
8-2-1943	?	0.0125 "	
9-2-1943	?	0.0125 "	
10-2-1943			
to			
12-2-1943	0.0	0.0125 "	Three daily doses.
13-2-1943			
to			
20-2-1943		Stopped	
22-2-1943			
to			
24-2-1943	Less than 0.1 to 1.0		Scanty normal parasites.
25-2-1943	3.4		
26-2-1943	1.4		
27-2-1943	0.2		
1-3-1943	3.6		
4-3-1943			
to			
12-3-1943	0.4 to 2.6		
16-3-1943	0.2		
29-3-1943	0.0		

(c) *Mepacrine hydrochloride in simian malaria*

Experiment no. 5.—Monkey no. 11, weighing 2½ kilos, showed parasites seven days after inoculation. It was treated with six doses of 0.0125 gm. from the third day of the patent period. The course of the infection is shown in table XI.

TABLE XI—*The course of infection in monkey no. 11*

Date	Infection rate of r.b.c. (per cent)	Treatment	REMARKS
22-1-1943	1.0	0.0125 gm.	Parasites degenerating. Very scanty degenerating parasites. Do.
23-1-1943	0.6	0.0125 "	
24-1-1943	Less than 0.1	0.0125 "	
25-1-1943	"	0.0125 "	
26-1-1943	0.0	0.0125 "	Two daily doses.
27-1-1943			
30-1-1943	0.0	Stopped	Scanty normal parasites.
5-2-1943	?		
6-2-1943			
10-2-1943	1.0		
11-2-1943	1.8		
12-2-1943	1.8		
13-2-1943	0.2		
15-2-1943	Less than 0.1		
16-2-1943			
to			
29-3-1943	0.0 to 0.6		Counts varied within these limits.

This monkey has survived a normal *P. knowlesi* infection as a result of treatment with mepacrine hydrochloride. Six daily doses of a smaller quantity of the drug did not prevent a relapse, though the parasite count during this period was appreciably lessened.

Experiment no. 6.—The incubation period in monkey no. 20, weighing 2½ kilos, was only three days. It was treated with three daily doses of 0.025 gm. from the fourth day after inoculation when the infection rate of the red cells was 5.2 per cent. The parasitological observations are given in table XII.

TABLE XII—*The course of infection in monkey no. 20*

Date	Infection rate of r.b.c. (per cent)	Treatment	REMARKS
6-3-1943	5.2	0.025 gm.	
7-3-1943	0.6	0.025 "	Degenerate parasites observed.
8-3-1943	?	0.025 "	Scanty degenerate parasites observed.
9-3-1943	0.0	Stopped	
10-3-1943			
to			
22-3-1943	0.0		
24-3-1943	0.6		Normal parasites reappeared.
26-3-1943	15.4		
27-3-1943	8.2		
29-3-1943	?		Died, showing 60 per cent infection of red cells in heart blood.

After treatment, the parasites were not seen in thin films for fifteen days. On 27th March, 1943, it looked as if the relapse infection was dwindling spontaneously, but on 29th March, 1943, the monkey was found dead, the infection obviously having flared up again.

Summary of results in simian malaria

Of six monkeys (*S. rhesus*) infected with a strain of *P. knowlesi*, which is so virulent that infection is invariably fatal if untreated, four treated with atabrine (Winthrop) and two treated with mepacrine hydrochloride (Bengal Chemical and Pharmaceutical Works) have survived the primary infection with this parasite. Both drugs have a destructive action on the forms of the parasite occurring in the peripheral blood. Relapses invariably occurred after three daily doses of 0.025 gm. or six daily doses of 0.0125 gm. It was noted that, in four out of five animals, such a relapse showed a secondary peak, followed by a natural decrease in the number of parasites leading to a chronic or latent phase.

Discussion

Mepacrine hydrochloride prepared by Bengal Chemical and Pharmaceutical Works, Ltd., Calcutta, has been found to be of value in the treatment of malarial infections of man, and observed to have physical effects of a varying degree, on all parasite forms occurring in the peripheral blood. Excepting the gametocytes of *P. falciparum*, *P. malariae* appears to be more resistant than the other two species, in that parasites persisted longer in the peripheral blood, although the infection was much lighter than in the case of *P. vivax* and *P. falciparum*. Morphological evidence of the destructive action of the

drug was comparatively scanty and less striking than in treated *P. knowlesi* infections. Part of the reason for this is that far heavier infections with the latter parasite are available for study. But it is also possible that the drug, in the dosage employed, has a more vigorous action on *P. knowlesi* than on the human plasmodia. It will be recalled that James (1934) demonstrated the direct effect of atabrine on *P. vivax* and *P. malariae*, and that Sinton (1938) has demonstrated its action on the gametocytes of *P. falciparum*, although, as is well known, the viability of the latter is unaffected. In one of the cases of *P. falciparum* infection treated in the present series of tests, evidence of the degeneration of young trophozoites was obtained.

Chopra, Das Gupta and Sen (1933) studied the action of atabrine on Indian strains of human malaria parasites. They found that, except for the crescents, parasites of all species usually disappeared on the fourth day of treatment. In one of the cases of *P. vivax* infection treated with Indian mepacrine hydrochloride, parasites persisted up to the sixth day of treatment, and in both the quartan cases, parasites persisted for about a week after the completion of treatment. These findings may be due to a more prolonged examination of thick films in the present study than in the work of Chopra *et al.* (*loc. cit.*), rather than to the superiority of the German product.

Chopra and Das Gupta (1933) studied the action of the original German brand of atabrine on *P. knowlesi*, and found it to be a powerful parasiticide. The atabrine prepared by Winthrop Chemical Co., U.S.A., is equally efficient. It has a powerful destructive effect on the parasites, and rapidly clears the peripheral blood of all forms. As with the German product, relapses occurred in every treated animal, the latent period being about eleven to thirteen days. Chopra and Das Gupta recorded latent periods of two to fifteen days. It would require precise experiments in which a number of variable factors involved are controlled, in order to prove that the latent periods after treatment with the two brands of atabrine are significantly different. The relapse rate was the same whether treatment was in three doses of 0.025 gm. or six doses of 0.0125 gm.

We are indebted to Dr. B. Mazumder of Messrs. Bengal Chemical and Pharmaceutical Works, Calcutta, for providing the mepacrine hydrochloride.

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THE OCCURRENCE OF ORIENTAL SORE IN THE HYDERABAD STATE

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H. E. H. the Nizam's Dominions

DURING a nutrition survey of school children at Pattan in Aurangabad District, my assistant, Dr. S. S. Ahmed, drew my attention to the occurrence, amongst the children, of chronic indurated sores of the skin and deeper tissues, and of shiny depigmented patches indicating scar-tissue of the healed sores. Later the same kind of sore was observed amongst school children at Jalna.

Pattan is a town with a population of about 9,000, situated about 40 miles from Aurangabad towards the South. Jalna is a big industrial town about the same distance to the East of Aurangabad. Its population is over 30,000. Aurangabad is situated at higher level than either Pattan or Jalna and is cooler than either of the two towns. Jalna and Pattan have many dense and congested localities.

Almost all infected persons stated that the sore began as a small pimple, red in colour, giving a sensation of itching. The papule was hard to the touch, and painless. It gradually increased in size and, after varying periods, the skin became shiny, smooth and bluish in colour. The tip of the papule was usually scratched off, and a sore with a white opalescent exudate resulted.

As a rule the sores are painless, but they may be very painful when the crust is removed for dressing, or when secondary infection occurs. The special feature of the sores is their chronicity. They do not respond to the repeated application of ordinary antiseptic dressing.

One attack of these sores appears to give complete immunity.

Incidence

The total number of boys and girls examined was 1,262; 79 had sores. The table below shows the percentage occurrence of single and multiple sores and their sites. The sex and community incidence is also shown.

TABLE

Total number of children examined	Total number suffering from oriental sore	INCIDENCE PER CENT BY CASTE AND SEX					
		Boys			Girls		
		Muslim	Hindu	Christian	Muslim	Hindu	Christian
1,262	79	6.6	10.2	2.9	2.8	3.8	Nil

The sores were mostly situated on hands, arms, feet, legs and on the face. The face, the forehead, the cheeks and the tip of the nose were generally involved. Sores on the face appeared to be more extensive and more destructive. A considerable number of children had multiple sores. The people of these towns recognized these sores as being of a special kind, and called them 'Chikni Punsī' because of their shiny and glossy appearance.

Smears made from material aspirated from the base of ulcers showed *Leishmania tropica*, thus indicating the occurrence of this form of cutaneous leishmaniasis in the Hyderabad State.

Clinical manifestations

The sores were seen in forms varying with the stage of the disease. Usually they were shallow, with crust formation, and discharging scanty red-coloured fluid. Most of the ulcers were roughly circular in shape. The edges were rough and protruding, and the base was covered with ashen-grey slough. These sores were usually about an inch in diameter; but sometimes two or three sores merged into one another to form an ulcer with a diameter as big as 3 to 4 inches. In poor hospital-patients, the ulcers were often in a septic sloughing condition and discharging pus, the surrounding skin being red and painful.

Incidence by case and sex

The incidence was definitely higher amongst Hindu boys and girls than amongst Mohammedan boys and girls. 63.2 per cent of cases had single sores; and 89.6 per cent of cases had sores on the extremities—hands, fore-arms and legs. Sores on the face came next in order of frequency.

Out of 79 sufferers, only 3 belonged to the richer classes. There is little difference in the economic status and nutritional conditions of the children of the Hindu and Mohammedan communities, the sanitary conditions in both groups being equally defective.

Laboratory findings

Smears of the material obtained by scraping the edges of the sores were stained and examined. Most of them showed streptococci, diplococci and staphylococci. It appears that in chronic sores with heavy secondary infection, it is difficult to demonstrate *L. tropica*. In early sores however, especially those in the papular form, material obtained by aspiration from underneath the base showed numerous *L. tropica*.

For these reasons, of 14 scrapings examined, only 4 showed *L. tropica*, though there was no doubt that clinically these were cases of oriental sore.

(Concluded on opposite page)

AN EPIDEMIC OF SMALL-POX IN THE KOLAR GOLD FIELDS AREA*

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Introduction

THERE was an epidemic of small-pox in the Kolar Gold Fields in the late autumn and winter months of 1942. A few sporadic cases had been reported since May 1942, but the disease took an epidemic form towards the end of October. One hundred and thirty-seven cases were admitted into the Epidemic Diseases Hospital during the following three months, November 1942, December 1942 and January 1943. An intensive study of 78 of the hospitalized cases, of which accurate and complete information was available, was made on the clinical side by one of us (B. K. R.), and on the epidemiological side by the other (C. V. N.). In addition, a study was made of the effect of oral administration of sulphanilamide on the course of the disease. The results of these investigations are reported herein.

Clinical

According to the histories, the patients were all admitted during the first week of fever; the temperature on admission varied between 102 and 103°F., and later rose in many cases to 104°F. A terminal rise of temperature was observed in three cases.

Almost all the patients came in with a papular rash which progressed to a pustular condition, and in a few cases the pustules became confluent or hæmorrhagic. Of the six cases which progressed to a hæmorrhagic condition, two recovered, both of them having never been vaccinated.

Sleeplessness and restlessness were noticed in all cases when the temperature rose to about 103°F. Delirium was a noticeable feature in 14 cases.

*The original manuscript has been condensed and partly rewritten. The findings indicate the need for revaccination.—EDITOR, I. M. G.

(Continued from previous page)

Further investigation to classify the sandflies and find out the vector are being made.

Acknowledgments

We are thankful to Dr. H. Hyder Ali Khan, Director, Medical and Public Health Department, for his permission to publish this report, and greatly indebted to Dr. M. Farooq, Deputy Director of Public Health, for his help in preparing the report.

Conjunctivitis occurred in 13 cases; the condition always cleared up under treatment, and no complications developed. There has been no case of dacryocystitis.

Nourishment had to be forced in 18 cases; mild dysphagia occurred in six of them; six children were too badly prostrated to swallow even fluids.

The case mortality rate was very high, being 33 per cent of all the cases studied; of the 63 previously vaccinated persons (mostly not re-vaccinated since infancy) 30 per cent died, of the 15 cases amongst unvaccinated persons 46.6 per cent died. Amongst the cases were three pregnant women, almost full term; they were delivered during the febrile period, and all of them died.

Treatment with sulphanilamide

All the cases were given sulphanilamide by mouth. The dose for an adult was 3 grn. per day; for children the dose was reduced according to age. Treatment with sulphanilamide was started at the height of fever, and was continued till the temperature came to normal and scabs started falling, or till the patient died. Sulphanilamide does not seem to have influenced the course of the disease, or the mortality rate. We have thus not confirmed the report of some other workers regarding the beneficial effect of sulphanilamide in small-pox.

Epidemiology

The majority of cases (45 out of 78) came from one locality, the Marikuppam area of the mining board.

As already stated the epidemic was seen in late autumn and winter months. In November 1942, the number of cases admitted into the hospital was 19, with a mortality of 31 per cent; in December 81 cases with a mortality of 31 per cent; and in January 1943, 37 cases with a mortality of 19 per cent. The epidemic subsided in February. More adults than children had been attacked. The age distribution of the cases was as under:—

Age group	Number of cases
0-4 ..	20
5-9 ..	9
10-19 ..	10
20-39 ..	36
40 and over ..	3

Of the 78 cases, 35 were males and 43 females. The distribution of the cases according to the different communities was as under:—

Community	Number of cases
Hindu ..	44
Mohammedan ..	11
Christian ..	23

Vaccination and re-vaccination is widely practised in the Kolar Gold Fields sanitary area; in view of this, the spread of the epidemic, mostly affecting the adults, is interesting. More than 80 per cent of cases (63 out of 78) occurred in persons who had previously been vaccinated; of these 63 persons, 45 had been vaccinated in infancy, 15 during the previous year and 3 during the fortnight before getting the disease. Although vaccination did not protect them from the disease, the case mortality (30 per cent) was lower than in the unvaccinated persons (46.6 per cent).

Summary

A study is reported of the clinical and epidemiological features of an epidemic of small-pox which occurred in the Kolar Gold Fields in the late autumn and winter months of 1942.

Sulphanilamide treatment has not been found to influence the course of the disease or the case mortality. Fatal cases deteriorated rapidly and died within 7 to 10 days of admission.

Acknowledgments

Our thanks are due to Dr. Krishnaswamy of the Epidemic Diseases Hospital for the careful records of the cases admitted into the hospital.

A Mirror of Hospital Practice

A CASE OF ACUTE MONOCYTIC LEUKÆMIA

By K. V. NAYAK, M.B., B.S.

Pathologist, K. E. M. Hospital, Secunderabad (Deccan)

THE patient, a male aged 55 years, fell ill on 2nd November, 1937. In the history there is nothing of importance excepting that the patient was a chronic sufferer from asthma and had suffered from hæmorrhoids for three years.

The present illness started with fever which was insidious in onset. There was no headache or any other symptom of note. The temperature for the first three days fluctuated between 99°F. and 100°F., but later varied between 101°F. and 103°F. and remained so till the end. The pulse was regular, its rate being 100 per minute.

Clinical examination.—The patient appeared moderately toxic with a low muttering delirium at times. There was no soreness of the gums but extreme dryness of the mouth was complained of; the tongue was dry and furred. There was slight bleeding from the nose, and a small quantity of sputum mixed with blood was coughed up once or twice in the beginning of the illness. A petechial rash appeared on both the forearms on 16th November which later turned maculo-papular and nodular. It was confined to this part of the body only. Slight œdema developed about the same time on the extensor surfaces of the forearms extending down to the

wrists. The liver was slightly enlarged and the spleen was just felt below the costal margin. There were no other swellings or glandular enlargements. There were frequent loose motions probably due to the laxatives the patient was receiving for his hæmorrhoids. The bladder occasionally became distended and had to be relieved by catheterization. Nothing abnormal was detected in the heart or in the circulatory system. There was slight congestion at the bases of both the lungs.

I was called in to examine the patient's blood for enteric on 16th when the inflammation of the hæmorrhoids had subsided and no symptoms referable to these were complained of by the patient. The Widal reaction was negative to the enteric group as also the Weil-Felix reaction to the proteus group of organisms. The blood smears showed no parasites, but presented such a striking picture of an intense non-granular leucocytosis that further investigations were made.

Blood.—Red cells, 4,500,000 per c.mm.; hæmoglobin, 80 per cent (Tallqvist scale), 12 gm. per cent (Newcomer scale), colour index, 0.9; corpuscular volume (corrected), 39 c.cm. per cent, this includes a leucocytic volume of 4.5 c.cm. per cent; white cells, 75,000 per c.mm.; polymorphonuclears, 0.5 per cent; lymphocytes, 4 per cent; monocytes (including immature forms and monoblasts), 95 per cent; myelocytes, nil; eosinophils, 0.5 per cent; reticulocytes, 1 per cent; Wassermann and Kahn tests were both negative. The sedimentation rate showed a great increase, with a first hour reading of 85 mm., a second hour reading of 120 mm., and a 24 hours' reading of 130 mm. (Westergren's method with a 200 mm. column at room temperature was adopted). The 'heterophil antibody' reaction of Paul and Bunnell with normal saline and rabbit's hæmolytic amboceptor as controls was negative. The urine showed only a trace of albumin.

Later history.—The patient was treated symptomatically; injections of prontosil were given but the condition became progressively worse; petechiæ increased in number, the tongue became swollen and the mouth sore. The liver started enlarging till it reached the level of the umbilicus; the spleen too was enlarged but its lower margin could not be clearly demarcated on account of abdominal distension. Congestion of the lungs increased and oppression in the epigastric region was complained of. Complete anuria set in later, and the patient died on 23rd November, three weeks from the commencement of the illness.

Summary.—The case is of importance in view of its extreme rarity and indicates the value of a routine examination of the blood in fevers of obscure ætiology without which the present one would probably have passed off undiagnosed.

I am grateful to Dr. G. S. Melkote, L.M.S.S., for helping me to work out the details of the case.



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Indian Medical Gazette

JUNE

'THE SOCIALIZATION OF MEDICINE'

A SURVEY of current medical literature of other countries reveals some interesting features. A prominent place is of course taken by articles dealing with medical and surgical conditions arising from the war, such as casualties in action and air raids. It is, however, good to see that clinical medicine is not neglected, that medical research is making great strides in certain directions, and that both clinical medicine and research are profiting in certain ways by the stimulus provided by war conditions.

But there is another and very important element in current medical literature, not entirely a new one it is true, but one that has greatly developed since the war; this element is made up of a mass of material bearing directly or indirectly on the future of medicine in all its aspects, medical planning, or 'the socialization of medicine' as it is sometimes called. This latter term is used both by supporters and opponents, and in these days it seems that the political views of the person using the term will determine whether approval or disapproval is indicated.

It seems to us that phrase 'the socialization of medicine' need have no political significance whatever. It should be an expression of the basic idea that medical services exist for the general good of the general population and not of certain sections, and it should also be a repudiation of the idea (rarely expressed but less rarely acted upon) that the public exists for the adequate support of the medical profession, and perhaps for the enrichment of certain members of it. The term 'socialization of medicine' surely indicates a process of development of medicine to bring it closer to the real needs of the people, and to develop the idea that the prime aim is to establish and maintain a high standard of general physical and mental health, and not merely to try to remedy defects or diseases when they have developed. The use of the term should also imply to the public that medical services have much more to contribute to their general well-being than the medical or surgical treatment of disease, which actually may be a small part of the service needed. It is very significant that chairs of 'social medicine' have recently been established in one or two universities in Great Britain, and that greatly increased emphasis is being laid on such subjects in the medical curriculum.

A survey of three of the important medical journals of England during the last six months of 1942 reveals the fact that, in spite of the reduced size of these journals because of paper

shortage, the references to the planning of the future of medical services number something like fifty, that they include editorials, original articles, reports and correspondence, and that numerous leaders of the profession are supporting the movement. It is obviously a matter which is regarded as being of great importance.

It is realized that medical policies in Great Britain may have little to do with medical work in India where conditions are very different. There are however certain facts to be remembered. In the past, medical training, hospital organization, medical practice, and health services have to some extent been influenced by the method and organization (or lack of it) seen in Great Britain, and some important features have been reproduced in a modified form in this country. This influence has acted sometimes to the good of medical work in India, but sometimes to its detriment. The curriculum of medical teaching institutions in India has too often and too closely followed that of similar institutions in England, and tropical medicine and hygiene have in the past been sadly neglected. The separation of the curative branches from the preventive branches of medicine has been reduplicated in India. The system of general practice and consultant practice has been adopted with modifications in India. The suitability of these measures to India is at any rate open to question. The medical services of India will have to develop on principles designed to meet the needs of India, and should not slavishly follow those of other countries. We should study methods used in America, China and Russia, Great Britain or any other country, and adapt what is good to our own country.

It does seem, however, that certain recent developments in other countries are of great interest even to those who may never be directly influenced by them, that there is occurring in Great Britain a very definite revolution, and that the next few years may see a complete remodelling of the conditions of medical work, following an already very marked change in the ideas underlying it.

No one can pretend to be satisfied with the present state of medical and health services in India. Sooner, or later, the revolution of medical work will come here also, and it may take a form quite different from that of the revolution now taking place in Great Britain, but we feel that a knowledge of what is being planned should interest our readers, and we reproduce in this issue an abbreviated form of a very important report on the subject which was published in the *British Medical Journal* a few months ago.

For many years in Great Britain, the more progressive of doctors have been dissatisfied with the conditions of general practice and hospital work intended to provide treatment for sick persons, and largely divorced from the health services which aimed first at the control of infectious diseases and now to some extent at

the maintenance of a good standard of health. Many doctors have been dissatisfied with the incompleteness and lack of organization and co-ordination of medical and health services. Various attempts to improve things have been made, such as the National Health Insurance scheme (which provided for wage earners but not dependants) and the hospital regionalization scheme (which attempted to make the hospital resources more generally available to those needing them) and so on, but these have been felt to be merely palliative treatment, and now more radical treatment is planned.

The details of the disorders from which the medical services of England are considered to be suffering and the general principles of the radical treatment recommended to remedy these disorders are discussed in the report mentioned, which is abstracted on page 309 of our present issue.

There are three striking facts about this report. The first is that the report was drawn up by representatives of the main corporate bodies of the doctors themselves, headed by the British Medical Association. The second is that the report is very frank in its discussion of the shortcomings of the different branches of the medical services, these shortcomings being largely attributed to the adverse conditions created by the lack of a co-ordinated plan. The third striking fact is that it makes definite proposals of a revolutionary nature, and encourages the adoption of some of these proposals almost at once.

This report appears to indicate a marked change in the views of a large section of the medical profession of England. It proposes to abolish or greatly modify the three main bulwarks of medical practice of the past, viz, the special status of the voluntary hospitals, the system of consultant practice sometimes called 'Harley Streetism,' and most important of all, the system of individual general practice, each practitioner working in competition with other similar practitioners.

It may be asked, What has brought about this change? We cannot answer this question in full, but there are certain factors which have certainly contributed. There is, no doubt, a marked 'shift to the left' (to use a medical term), in the views of a great many people in Great Britain. There has always been a considerable number of doctors who have held views which may be generally described as 'socialistic', and that number seems to have increased; (there is a strong and influential socialist medical association headed by eminent members of the profession). Many other doctors, while perhaps not being politically socialists, are in favour of the practice of such principles in medicine.

Numerous doctors in Great Britain have in recent years visited Soviet Russia, and some have published very favourable accounts of the achievements of the state-organized medicine incorporating both curative and preventive work

in that country. Such writers, by the way, have included one retired Director-General of the Indian Medical Service. All these facts have helped to mould opinion inside and outside the medical profession.

The report abstracted in our present issue is not however the work of a few enthusiasts, but has been prepared by a very carefully selected representative body including all shades of thought, and all branches of the profession. The report has moreover been adopted by the Annual Meeting of the British Medical Association.

It appears that there is little or no difference of opinion regarding the general type of medical service that is needed, or on the general lines of its organization. The main difference of opinion has been regarding the best method of administration. Two general methods have been considered. The first is the organization of a state medicine service by a state department. On this basis, all practising doctors would become Government servants. The second method is the organization of the scheme by a representative corporate body, not a state department but responsible to the state. This latter method was favoured by the majority at the British Medical Association meeting, but the former method seems to have been recommended by Sir William Beveridge in his social security scheme prepared at the request of the Government and now under their consideration.

We hope that all our readers will read the report either in the abbreviated form in our present issue, or in the full form given in the *British Medical Journal* (June 20, 1942, p. 743).

So many of the faults of the medical services in England so frankly discussed in the report are seen perhaps in an even more serious form in India. Are any of the remedies suggested applicable to India? At present it is obvious that many of them are not, but we think that the idea of the 'health centre' staffed by a group of practitioners and undertaking the wide range of activities outlined in the report may be applicable in some urban areas in India. Moreover, we are quite sure that the aim of future developments in India should be to create conditions such as will favour the application of the general ideas outlined in this report.

J. L.

Special Article

A PLEA FOR A MORE COMPREHENSIVE OUTLOOK ON THE HUMAN BODY

By A. INNES COX, O.B.E.
LIEUTENANT-COLONEL, I.M.S.

Divisional Medical Officer, Nilgiris

In a previous article in this Journal (Cox, 1941) I voiced a plea for a more comprehensive outlook on the human body, believing, as I do, that much is missed by the admittedly necessary

specialization of to-day. It is indeed unfortunate that life is so short that no one can survive long enough to be a specialist in all the branches of medicine and the allied sciences.

In what follows, I attempt to lead the reader to a realization of the necessity of an even more comprehensive view of life. The idea I have in mind is the necessity for the pooling of all knowledge available with the anatomist, biologist, veterinary surgeon, odontologist, geologist and physician. Perhaps in the remote future, man may acquire sufficient cerebral power to embrace all this knowledge, but at present it is not possible, nor even is intercourse with such as have a knowledge of these subjects possible in a remote corner of India. I need therefore offer no apology for inaccuracies and speculation.

Science has suffered seriously during the last one thousand years on account of the difficulty man has experienced in breaking away from the thought-patterns of his forbears, for the various beliefs prevalent in the world have been in no small way responsible for the retardation of understanding. Men have for a thousand years sought to fit the facts of life to their beliefs, rather than base their beliefs on the facts of life. It is indeed but a short time since emancipation from the fetters of dogma has allowed of free thought without penalty. I need only recall the Inquisition, the fate of Copernicus, Giordano Bruno, Galileo and a host of other thinkers, not to mention the controversy that arose over Darwin and even more modern pioneers of scientific discovery.

However, we are now free to think, and I ask the question: Is Man the masterpiece of creation, or is he singularly imperfect? If man is a final perfection, then why do we doctors see so much suffering? If imperfect, in what direction is man progressing towards perfection?

Let us free our minds from the thought-patterns woven by our upbringing, and project ourselves to such a distance from the world as will allow of a proportional view of all life in the animal kingdom, in the almost infinity of time that is past, in the present, and in the infinity of time that is to come, see what impression we get of the species *Homo sapiens* and decide where we are to place him in the evolutionary scale.

We should I think, without undue surprise, regard life as springing from some of the permutations and combinations of possibilities resulting from the interaction of the inorganic elements in an electro-magnetically and radioactive world, and recognize that life does not originate at 'a beginning' but as a continuous sequence of events.

We should see, in panorama, all stages of development, from the sub-kingdoms protozoa and metazoa to the final species, some perfected and others developmental. In the past we should see innumerable species now extinct; in the future, species to come, and extant species passing on to an optimum, and dying out from the earth.

In an infinity of time past, an infinity of forms of life must at various times have been possible, but in the present, no. In the present there is an all-powerful veto on life that we may term 'environment'.

Environment, which is ever slowly changing in the eons of time, has a powerful control over life, and over the surface of the earth environment differs; hence do forms of life differ. One need only call attention to the environmental differences between life in the sea and life on land, life near the poles and life near the equator, and all the degrees of change, infinitely small, between these extremes, to realize that forms of life, once life is started, must be almost infinitely numerous. But all forms of life do not attain to a growth of any appreciable size. Lowly forms like the amoeba may undergo but little environmental change, and so remain content in their degree of perfection, awaiting only some change either to bring about their extinction, or to force a modification into some kind of the more efficient metazoon.

On the other hand, life that has struggled against constant environmental change over millions of years, may have achieved such perfection in a particular line of development as to be incapable of further improvement. This may well be the case with the extinct mammoth, which, with its perfect tusks up to 13 feet in length and 200 lb. in weight, strongly curved, forming a considerable segment of a circle, failed to further modify itself in accordance with the demands of changing environment and died out. On the other hand, its modern analogue, the comparatively straight tusked Indian elephant, less perfected, has been able to survive to the present day.

One could cite a number of such cases of growth, development, perfection along some particular line, followed by extinction; but what better example than the giant tortoise, which, with its rigid shell of nearly half a ton, perfected in defence until its leg muscles failed to hypertrophy with the weight of armour, which, unable to develop further because of it, collapsed and died out, not only ossified, but literally keratinized. Its modern analogue, the leather back, has no such restriction, for its backbones have not yet joined, this fact permitting of even greater growth of the species.

True, these are but stories, but these stories clear the viewpoint I wish to set forward; for viewing the animal kingdom thus, one cannot avoid the conclusion that each species having selected a particular organ for special development in its struggle for existence, has pursued, or is pursuing its selected course up to and until it achieves an optimum; and then perfected, is unable to change in accordance with the demands of its changing environment, and either dies out or is killed off by enemies that have developed more efficient weapons of offence.

From this imaginary viewpoint, I can see no evidence that any species, having once developed

an organ for its own preservation, and having come to the realization of failure in its purpose, has been able to change over to another line of specialization. To do so would presuppose the change of one animal into another. The point here is that perfection in the development of an organ or group of organs heralds the senile decay of a species, and there is no evidence that the species *Homo sapiens* is near decay. On the contrary, it suggests that man has as yet far to go before reaching the optimum of perfection.

Many forms of life are similar in appearance and action, and on this similarity the systematist bases his classification of the animal kingdom into sub-kingdom, grade, phylum, sub-phylum, class, order, family and so on, but nowhere is there evidence of one species developing into another. Hence there is no need to hold fast to the idea that man has evolved from monkeys. It is more probable that monkeys and apes have progressed so far in their specialization as to have lost for ever their chance of becoming man. But sure it is that man has developed through simioid forms from creatures even more primitive than the tarsius, and has much that is primitive, in fact almost reptilian in his present make up, for Professor Wood Jones proves very conclusively in his book *Arboreal Man* that the arm and hand of man has never been wasted as a body-supporting agent, but that the arm and hand have retained the form and freedom of their very early amphibian state.

It is possible that man as we know him to-day is a species similar to the cro-magnon man and/or pithecanthropus, and not necessarily a development of those man-like creatures. *Homo's* ancestors may have been too poorly ossified to permit of preservation. Man may indeed be more embryonic in the span of his species than any of his off-time supposed immediate ancestors, and comparatively new in the scale of life, indeed almost foetal in structure in relation to his potential. This idea is, to some extent, supported by the fact that one-third of the life of *Homo sapiens* is spent in growth, the delayed ossification permitting of considerable further adaptation to future changing environment.

From such a view of life it would appear to be more a matter of proportional degree of development to possible perfection of development along one line that determines the future span of a species before final extinction, rather than the gradual efforts of nature under the guidance of a supreme being to produce a perfect creation that we are pleased to call *Homo sapiens*, destined to survive the extinction of all else; for homo to the physician is far from perfection, either in form or structure, as evidenced by the multitude of reparative operations now grouped as classical. Is it possible in the present stage of evolution to forecast the changes that are likely to take place in the future, and if so, can these changes be accelerated and assisted, or the disabilities of the transition ameliorated?

For it appears possible that the species man in its present stage of development in the life-span of the species is at a point where instinct is at an ebb, and reason has not yet developed sufficiently to replace it; a dangerous period comparable to that of a child of seven years, who, lacking the guidance of parents, experiments for itself.

If the physician realizes that he is not dealing with a perfect organism, and if he is able to form a correct idea of the line of development selected by the species, then only will he be able to teach reason to his fellow creatures, and offer true guidance. At present one hears, only too frequently, reference to conditions that obtain in sub-human types, thus presupposing the human type to be the latest evolutionary development. Science challenges this, for sub-human types may well be a distinct advance on the human, so far as the mechanics of the animal are concerned.

For this reason, I essay a comparison between the alimentary systems of two perfected types, the carnivorous and the herbivorous on the one hand and *Homo sapiens* on the other. The study is interesting, for at present large numbers of the species homo are meat-eaters, and large numbers either from economic necessity or mental persuasion are herbivorous, and my experience with both types leaves me without any doubt that there is much more suffering and illness among the latter. Also the following comparative study points to what is the nearest approach to a proper diet for man in his present stage of development, by showing how closely man's alimentary canal approximates to that of the truly carnivorous animal.

Let us make a brief survey of the alimentary tract of man, beginning at the mouth. The skin that covers the surface of the body alters its character only to become the mucous membrane at the lips, and the teeth are but a modification of the epidermis. This is clear in the case of the shark, where the dermal hooks, turning up on end as they round the margin of the jaw, hypertrophy as a result of the sudden extra use (and hence extra blood supply) and form a continuous series of primitive teeth. This fact is not readily recognizable in, say, the elephant, yet the process is the same, and can be traced in the early embryo, for the enamel organ remains epithelial, only the pedestal on which it stands, and which later grows into it, being the secondary result of a demand on the mesoderm of a fixed base.*

The tooth of the shark is primitive, like its elasmobranch owner. The tooth of the elephant, like its owner, is nearly perfected for its use.

In what stage between the primitive and the perfected, is the tooth of man? The teeth of man are 'bunodont', that is, they have rounded

* Does this not suggest that vitamin A would be of more benefit than D, for developing teeth capable of resisting caries?

cusps set upon short roots, diphyodont and not persistent growing. They are modified neither for chewing the cud, nor for killing large game. The teeth are simple teeth, and are capable of considerable modification if necessary, or they may remain unwanted and so become reduced in both size and number. The analogue of such simple teeth is found in fossils as far back as the cretaceous period of mesozoic times, when life was primitive and probably entirely reptilian, and, as in the case of the fore limbs of man, there has been but little change. Such a primitive state of affairs of the teeth is to be expected, for hands of primitive mobility can relieve the teeth of much of the work required of them. A monkey can catch a bird and kill it with its hands; a dog can catch a hare only with its mouth, and kill only by use of a mouth in which it has grown specialized teeth. So in man, who has retained the primitive mobility of the fore limb, and acquired a brain with which to make use of that limb, the teeth have remained primitive in the absence of a specialized use for them.

Then the mouth of man is simple. The tongue is free, to permit of speech in accordance with the demand of the developing cerebrum, but as an organ of alimentation it is a poor article. Compare it with the tongue of a herbivorous animal. There are none of the enormously hypertrophied rasping papillæ, neither can it grasp articles of food. The mucous membrane of the lips and cheek is smooth. This is not so in the case of the tongue and cheek of the well-developed herbivora.

The oesophagus in man is a simple tube; there is no modification comparable with the crop and gizzard of herbivorous birds.

Then that important organ the stomach. In homo it is very simple dilatation of the alimentary tract, showing but little specialization. It is of comparatively small capacity, so presumably the animal man must be selective in diet and not waste space.

The secretion is of a fairly strong hydrochloric acid, and this fact, with the small capacity, suggests that it is intended for a diet rich in protein, yet consisting not wholly of animal flesh, as it is insufficiently specialized, more closely approximating to the insectivorous and seasonal frugivorous animals of the order Primates. It is indeed far from showing any modification comparable with the typical herbivorous animals.

Considered physiologically, in the typical 'carnivorous' stomach, and in the stomach of man, the gastric hydrochloric acid is high, 0.4 to 0.6, while in the 'herbivorous' stomach it is from nil to 0.13. In the carnivorous animals and in man, roentgen ray studies show that the empty stomach is contracted and tubular, bent upon itself at the junction between the fundus and the pylorus—the incisura angularis. Moreover, this type of stomach is seen to empty completely between meals. In the typical herbivorous animal, the stomach is

highly specialized, and where the stomach is less obviously specialized, there is compensation in a specialized colon and an enormous cæcum, called a 'floating cæcum', as in the horse.

For instance, in the cow, the rumen is relatively enormous, filling nearly three-quarters of the animal's abdominal cavity, while in the horse, where the stomach has not attained the same degree of specialization, the colon has developed, and with it there is a relatively enormous cæcum. The colon attains the capacity of some 16 gallons, and the cæcum up to 8 gallons. It is in these enormous natural fermentation vats that cellulose is digested and converted into glucose, not by enzymes poured out by the animal, but by some enzymes contained in the vegetable food itself (cytases) and by bacteriological fermentation. Only thus is cellulose utilized by the vertebrate species. Again, only the carnivora and man empty their stomachs between feeds. The herbivora never empty their stomachs: in fact it is found necessary to starve some herbivorous animals up to five days to empty the stomach, after which time there is danger of death from starvation unless there is some other specialization, as in the camel.

CAT



Fig. 1.—Typical carnivorous alimentary canal. Simple stomach. Relatively small and short. Small intestine. Cæcum small. No appendix. Large intestine, small and short.

COW

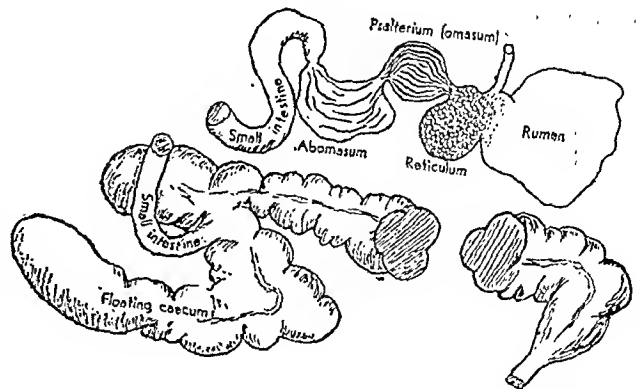


Fig. 1a.—Typical herbivorous alimentary system. The first three compartments of the stomach are for maceration and fermentation and occupy three-quarters of the abdominal cavity. Small intestine voluminous. Large intestine relatively enormous. Cæcum very large to complete cellulose digestion.

Many of the carnivora are unable to subsist on a diet other than flesh; this is the case with

the tiger and lion, and in the natural state these animals choose the herbivora for the ideal diet, possibly on account of the acquired ability of the herbivora to utilize plant life in building up

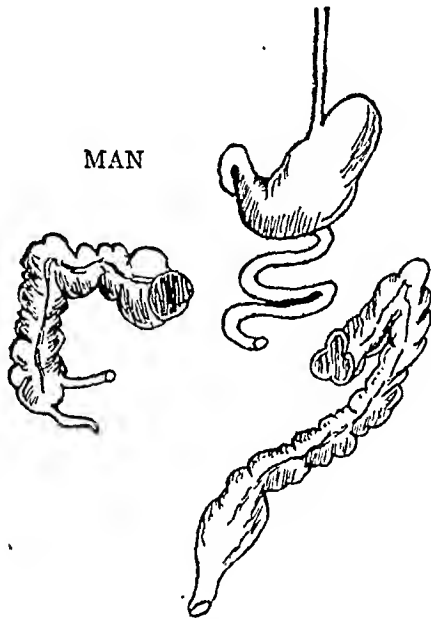


Fig. 1b.—Simple stomach. Relatively small and short small intestine. Medium to small large intestine. Small caecum and appendix.

their necessary store of vitamins. Others, like the dog, ean, albeit with detriment to their health, subsist on a mixed diet. Here I recall the fact that I, when a student, kept a sheep dog in London, and with the mistaken idea of keeping the animal docile, I fed it on biscuits and rice, with the result that it developed diabetes and carbuncles.

Man can subsist on either or both diets, the Esquimo being wholly carnivorous, and many in this country being wholly herbivorous, a mixed diet rich in protein being generally acceptable.

We now pass on to the small intestine. In the typical carnivorous animal, the small intestine is relatively short and of small calibre, as would be expected where the diet requires little more than the breaking down of ready-made animal tissue, and its absorption prior to re-synthesis. But in the herbivora, relatively massive quantities of food are required to obtain the basic requirements of nitrogen; hence an enormous absorptive surface is essential, and for this reason the small intestine is correspondingly large.

In the large intestine, great differences are again apparent. In the carnivora the large intestine is comparatively small, the caecum rudimentary, and the appendix but a dimple; it can indeed be said to be absent. In the herbivora, the large intestine is voluminous and in those animals which have not developed stomachs specially modified for cellulose digestion, the caecum is developed to massive proportions, and is known as the 'floating caecum', and, except in the rabbit, there is no appendix. In the rabbit, however, there is a

large caecum, and a large appendix that may well be opening out to form a complete floating caecum as in other herbivora, as it approximates to full development, from a rodent to a true herbivorous animal (see figure 2).

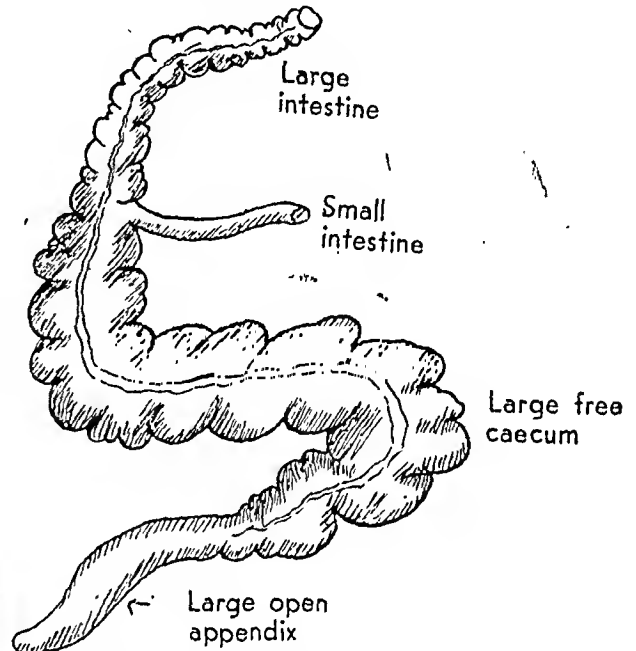


Fig. 2.—Caecum and appendix of a rabbit.

In man the large intestine approximates to the carnivorous type, with the exception that it is comparatively large, and there is a caecum and an appendix. It is of interest here to note that the *Science of Life* by Wells, Huxley and Wells (1937) describing the caecum, appendix, and large intestines of man, states: 'In man these structures have no functions that other organs cannot carry out—indeed, it is probably better to be without an appendix, for it may be the seat of acute and even fatal inflammation. It is improbable that the human large intestine plays any important part in digestion. People can live to be healthy and active after its removal, etc.' Certainly Lane was an enthusiast for its removal. But early natural man was not concerned with the necessity of being prematurely pitchforked from a carnivorous species into a herbivorous.

Keith (1920) states: 'In all the higher primate forms, we note, on the right side of the abdomen just above the groin, that the small intestine ends in a capacious caecum, the name given to the dilated commencement of the great bowel. At the closed and lower end of the caecum in the anthropoid, as in man, is attached a narrow tube, the notorious vermiform appendix. It terminates bluntly below, and hangs freely within the abdomen, lying more or less behind the caecum, into which its upper end opens.

'It varies in size according to the age of the individual and state of digestion.

'In the gorilla, it is of the thickness of the small finger, but twice as long; in man it is shorter and smaller, but in him its shape and

size are subject to the utmost variation after puberty.

'Unfortunately we do not know the uses of the appendix, but on many occasions the writer has noted in the anthropoids, and in children, that the contents of the cæcum pass freely into it.'

This opens the possibility of man's cæcum-cum-appendix being in reality a developing floating cæcum, the appendix being the undilated projection of a slowly dilating cæcum. Certain it is that the appendix in a child is much larger and longer than it is in an adult, and, I am inclined to think, the cæcum correspondingly smaller. The whole picture is that of child's sausage balloon half blown up. It looks like this :—



Fig. 3.—Half inflated sausage balloon like a cæcum and appendix.

Fully blown up it looks like this :—

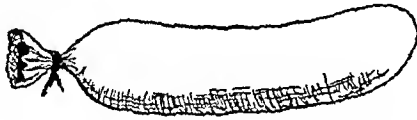


Fig. 4.—Fully inflated balloon like a floating cæcum.

The first is the cæcum and appendix of modern man, and the second is the floating cæcum of the fully develop herbivorous animal. Is not the appendix of man possibly the sign post pointing in the direction in which the development of man's alimentary canal is taking place, an index of the belated struggle of man's alimentary canal to evolve into a more herbivorous type ?

If the alimentary system of man really is but little more than foetal, (and the rule in nature seems to be the suppression of development of all organs not immediately concerned in the developing speciality), and like all foetal animals carnivorous, then we may expect the major digestive glands to fail when they are plied with a diet for which they are not yet modified. The two large organs, the liver and pancreas, immediately come to mind, and we may confidently expect their failure from causes other than specific diseases.

Those of us who practise medicine in India will immediately think of the large ample-bellied unfortunately strict sectarian who, vegetarian from the time that he was weaned, suffers from either hepatic or pancreatic failure or both at the early age of 40, and from a blood pressure to correspond, resulting from thirty-nine years of vascular irritation from an abnormal blood sugar, the result of a diet of starch, for the reception of which his alimentary system has not yet been developed. It is

known that in the herbivora, glucose feeding causes less hyperglycæmia and consequent exogenous glycosuria, than in animals with simple stomachs. In practical support of this, I again recall my dog story mentioned above. The cause of death may, of course, have been pure vitamin deficiency, but a well-fed dog seldom calls for vitamins. Vitamins may have helped the animal to exist under the abnormal dietary conditions, much as we too try to compensate for our dietary conditions, to-day by covering the breakfast table with potted vitamins.

Another point is that the carnivorous stomach is allowed to empty between meals. This gives the liver time to distend to the maximum, and then, as it were, to deflate, thus permitting of a good flushing with an unimpeded blood supply. The overgorged vegetarian stomach is never at rest, and the liver is never permitted to discharge its overload of glycogen, with the result that it is seldom or never allowed to relieve the engorged pressure against its inelastic capsule. The delicate reticulo-endothelium is robbed of its free blood supply, the venous channels are compressed, while the arteries maintain their calibre. Venous stasis and engorgement result, and the end is not surprising, namely a classical hypertrophic cirrhosis.

The body of man has a small alimentary system compared with that of the herbivora ; hence if the food is mainly starch, cellulose and roughage, the call for more and yet more nourishment may well become irresistible ; more food will be taken, and the stomach will be further gorged until the compensatory efforts of nature, namely hypertrophy and dilatation, fail, and atonic dilatation with a sour fermenting decomposing content remains ; belching of wind, (a bi-product of fermentation), constipation, and starvation result to complete the picture. All these symptoms are only too evident in a vegetarian population, and are dubbed the 'evils of civilization', to be relieved by the prescription of more 'roughage' in the hope that the gut will be irritated to the stage of a mild irritating diarrhoea, which naturally brings a measure of relief by getting rid of what should never have been there.

Another not uncommon manifestation of the inability of man's alimentary system to deal with cellulose, is the occurrence of 'ragi obstruction'. Ragi is a small grain with a hard pericarp. Man has no rumen nor floating cæcum in which to digest this by the process of natural fermentation ; hence the irritation of the cellulose gives rise to spasm so severe as to render the intestinal canal identical in appearance with a string of sausages, and a clinical picture indistinguishable from that of advanced intestinal obstruction is produced.

Still further, in the frugivorous and insectivorous birds, the gut is very short, while it reaches its maximum length in the grain-eating birds.

Recently Dr. Aykroyd gave me the opportunity of examining the belly of a *Macacus sinicus* monkey. The following diagrams were sketched from the appearance presented. A glance at the sketch will show that this little creature has become almost entirely herbivorous; indeed Dr. Aykroyd tells me that he cannot get this type of monkey to eat meat. It is seen that, although the stomach is simple, very like that of man, the large intestine, the cæcum, and the appendix are purely herbivorous. The haustrations stop short at what appears to be the end of the original cæcum, and beyond this is a smooth sack just as would be expected were an appendix to be inflated. Has this little animal attained the optimum of its evolutionary development, the optimum at which man is aiming as regards his alimentary system? It looks very much like it.

Another interesting point about this dissection is the fact that the animal was out of condition (the reason for its destruction); the disability was an enteritis.

Now the cæcum shared in this enteritis more strikingly than the rest of the gut, and from it there ascended to the pre-aortic glands just such a lymphangitis as I described in my previous article. The enlarged and pathological glands arising from the cæcum increased in size as they approached the pre-aortic glands at the root of the mesentery, where there was one large suppurating gland. Had that monkey been able to talk, I am sure it would have complained of appendicitis, and discomfort relating to the epigastrium as I have described, and had it been human and so treated on general lines with recovery, it would, after a long period of years of discomfort, have been subject to all the complications described, including volvulus, as the lines of lymphangitis became scars, and contracted, giving rise to the various obstructive points that I enumerated. But this is wandering from my theme. To return, Elliot Smith states on page 30 of his *Essays on the Evolution of Man* '... It is the steady growth and specialization of the brain that has been the fundamental factor in leading man's ancestors step by step upwards from the lowly insectivorous status, and through every earlier phase in the evolution of the mammals ...'

Man has specialized in the development of the cephalic end of his anatomy, and a broad survey of the animal kingdom strongly suggests that any animal, having once selected a particular organ for development for its preservation, pursues that course up to an optimum of perfection, and then, being incapable of further modification, should environmental change demand, gives place in the world to a species more youthful, less perfected, but of much greater potential.

While he has been specializing in a cephalic perfection, man's other organs have lagged behind, subservient to the one great branch of growth, the brain, and I suggest that man's

body in general, and the alimentary canal in particular had remained primitive and unspecialized, showing but little change since the days

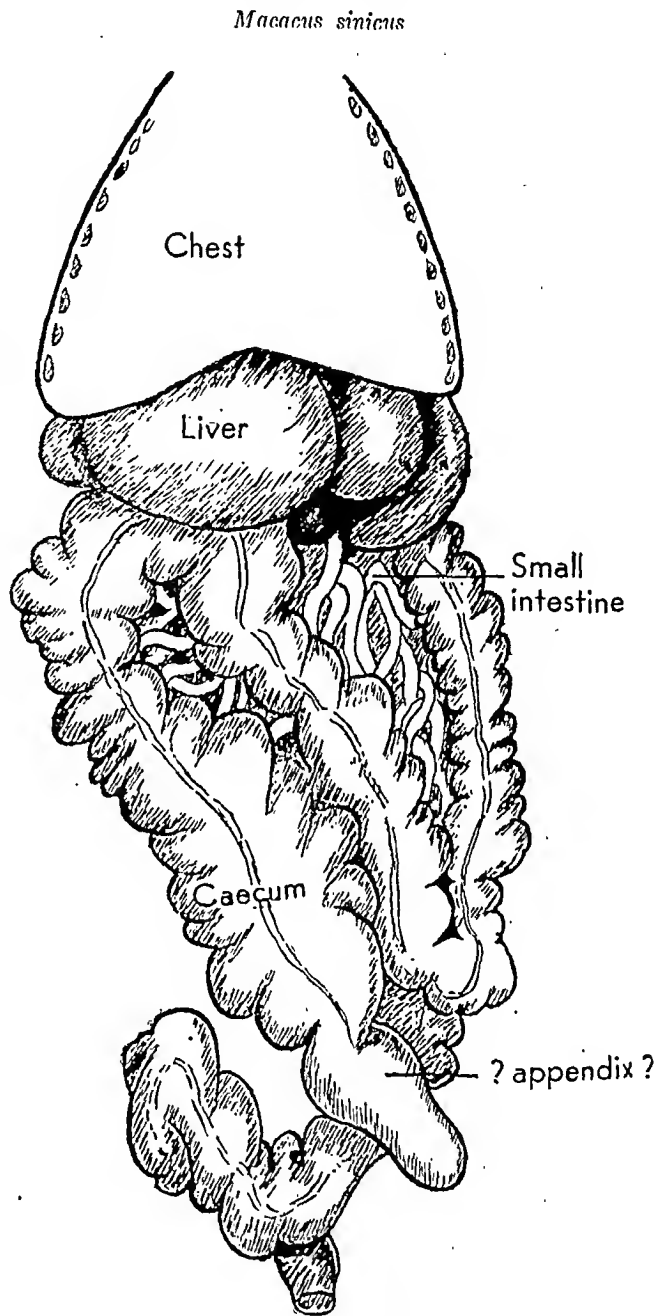


Fig. 5.—Natural position.

of an insectivorous (carnivorous) and seasonal frugivorous modification, ill-adapted to the environmental change forced upon it by present-day economic and religious necessity, whereby it is compelled to become vegetarian and granivorous. It is thought that milk may supply the absent animal protein and fat. But again the infant stomach only is modified for milk by the secretion of rennin, whereby the milk is rapidly solidified and so retained in the stomach sufficiently long for acid digestion. In the adult, milk quenches thirst; that means, that milk being

fluid, rapidly passes through the stomach into the intestines, where, in an alkaline digestive medium, it cannot be adequately digested, and so it gives rise to flatulence, distension and diarrhoea, the constant complaint of the hospital patient who, unused to a diet of milk, complains that it causes such discomfort that he cannot take it; this too is my own experience on a diet of milk. Hence I challenge the belief that milk is a perfect food for anyone but the

not tolerate anything egregious. It is probable therefore that the species man has suffered but few and slight, if any, changes by mutations since the days of reptiles.

Speculation on man's past, present and future is likely to remain speculation until sufficient recorded time is past, possibly millions of years, but sufficient knowledge of the past may be unearthed to permit of the establishment of a sense of direction; and of the sciences, a comparative study of the animal kingdom is likely to be the most fruitful.

The subject of dietetics has received much attention of late. The fact of a high protein content of a cereal is recognized as some measure of its value, and by finding a cheap diet, mainly vegetarian, compensated by the host of vitamins,

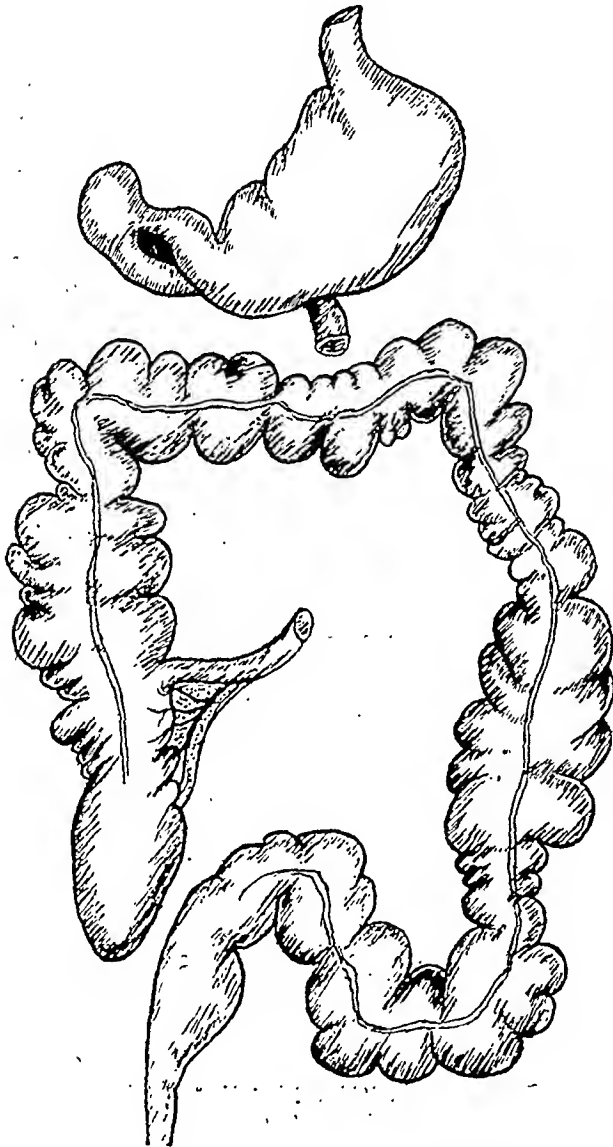


Fig. 5a.—Stomach and large intestine spread out.

infant, who is able to submit it to true gastric digestion by virtue of its rennin secretion.

In the light of the above suggestions, would it not be profitable to further pool our knowledge of the sciences, and include at least a survey in the student's curriculum? The genetic specialist may be able to throw light on the natural changes that take place in nature by some form of mutation, but it is probable that mutation plays only a small part amongst the more developed of the animal species, and least of all amongst herd species, for the herd does

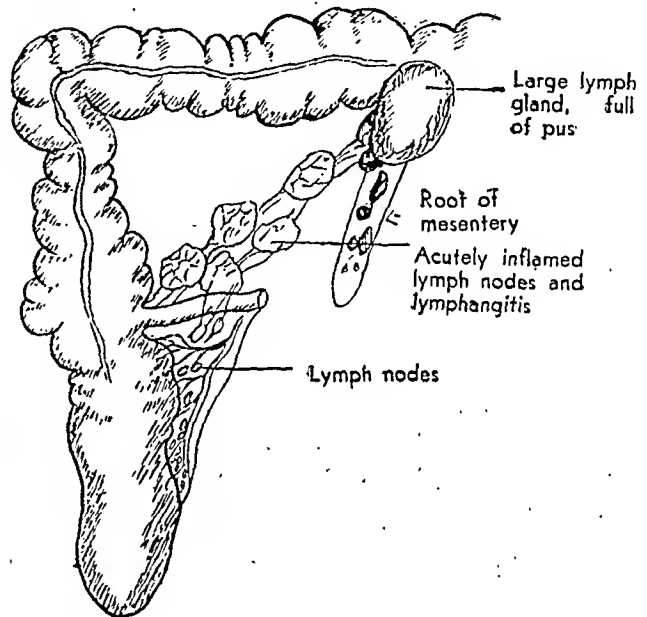


Fig. 5b.—Cæcum and appendix showing the ascending lymphangitis from inflammation in the cæcum and 'spread out' appendix of the monkey.

it seems to me that we seek to accelerate the environmental change, (whereby man is to live by the plough rather than by the chase), so rapidly that nature is unable to modify the anatomy and physiology of the species at the rate required by man-made economic conditions.

The tendency now is to calculate the capacity of a land to maintain a population by its herb-producing capacity. 'Grow more food' refers to vegetables, wheat, rice and so on, while cattle are crowded out; yet insects and herbivorous animals are the natural protein and vitamin factories, and man is not. Are we sure that man with an alimentary system so little developed as to be more 'proteinivorous' than 'carbohydrate-ivorous' will not suffer progressively for want of the many by-products of protein metabolism? I mention only one, urea. In my previous article I stressed the clinically anæmic and hydræmic state of a number of the poorer class of patients who suffer from a permanent

state of lymphatic catarrh, a 'naso-oro-pharyngileus', as an able colleague of mine once aptly dubbed the condition, and I endeavoured to trace to this source the prevalence of tonsillitis, granular pharyngitis, Payer 'patchitis', appendicitis and the abdominal glandular adenopathy so prevalent amongst a poor and hence herbivorous population, albeit living on a soil rich in iron and manganese (laterite). Is it not possible that the discovery of vitamins has to some degree thrown dust in the eyes of the physician, and blinded him to the prior need of animal protein? The fact that a grain has a high vitamin content is no criterion of its nutritive value, for a grain may be quite unsuitable for the alimentary system of man, the quondam carnivorous, as in the case of small grains like ragi, hill paddy (chamai), kumbu or even cholam, for those of us who practise in the south where these grains are used, are only too familiar with the difficulty of diagnosing a serious abdominal catastrophe from a small grain 'obstruction'.

Is it not possible that urea, a by-product of protein metabolism to man, is essential in his present state of development not only as a diuretic, but also as one of the more potent natural antiseptics necessary to combat infection?

Urea has with advantage been used as a dressing for wounds. A high protein diet is invariably considered desirable in tuberculosis, and urea is only one of the products of nitrogen metabolism.

Is it not also possible that the prevalence of gastric ulcer, of the classical 'peptic' type so common nowadays, is due to the failure of man to consume sufficient animal protein, which, alkaline in reaction, is able to neutralize the acid side of digestion?

Where then should we place *Homo sapiens* in the evolutionary scale?

The facts seem to suggest that no animal can be typed and placed, for we must admit that, when cerebral development is considered, man is the highest attainment; but when the alimentary system is considered, man is far down the evolutionary scale.

If tooth and claw be considered, the tiger probably leads; if speed, then the horse may be near the highest attainment.

And so, it is not possible to consider man as a whole. The perfection of creation is but a jumble of organs in various stages of evolution, some highly specialized and others elementary and rudimentary.

The artificial separation of medicine and surgery (said to date from Avicenna A.D. 1000), has given rise to two professions, and, later, specialization has given rise not to two professions, but to a dozen.

These divisions must be bridged if man's anatomy, physiology and pathology are to be properly understood; this idea calls to mind the fact that as far back as 1904 Sir Clifford Allbutt

wrote: 'As we cannot know any part of an age or people without an idea of the whole, nor take to ourselves a lesson from other times of other folk without some conception of their nature and fashion, so we cannot know modern medicine unless we study it as a whole, in the past as well as in the present.'

From Greece, and mediæval Italy we have to bring home the lesson that our division of medicine into medicine and surgery had its roots not in nature, nor even in natural artifice, but in clerical, feudal and humanistic conceits.

I remember reading that Sir Clifford Allbutt advocated a professorship in comparative pathology some 60 years ago. It is indeed true that we must widen our horizon from the study of man the perfect to the study of man as one member of the animal kingdom.

It is probable too that we shall run our course to an optimum of perfection, without doubt, lengthened by our cerebral capacity to mould environment to our needs, again to an optimum, and then, having established a record for the animal kingdom, die out and make room for a fresh cycle of evolution.

I acknowledge with appreciation the help so freely afforded me by Dr. Govindan Nayar of the Madras Veterinary College for his kindness in checking the accuracy of my remarks about the typical animal types of digestion, and for correcting any inaccuracies.

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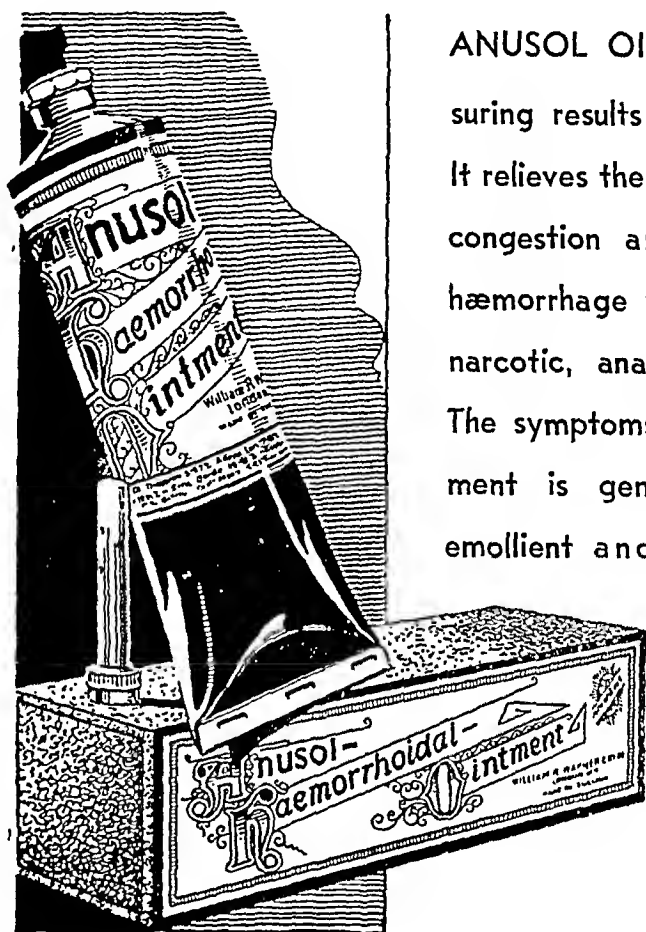
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Public Health Section

MEDICAL PLANNING COMMISSION

DRAFT INTERIM REPORT

(Abstracted from the *British Medical Journal*,
20th June, 1942, p. 743)

INTRODUCTION

THE Medical Planning Commission was established by the British Medical Association with the co-operation of the Royal Colleges and the Royal Scottish Corporations in August 1940, with the following terms of reference:—

'To study wartime developments and their effects on the country's medical services both present and future.'

The bodies appointing to the Commission, which consists of 73 members, are the British Medical Association, the Royal College of Physicians of London, the Royal College of Surgeons of England, the Royal College of Obstetricians and Gynaecologists, the Royal College of Physicians of Edinburgh, the Royal College of Surgeons of Edinburgh, the Royal Faculty of Physicians and Surgeons of Glasgow, the Society of Medical Officers of Health, the Faculty of Radiologists, the Medical Women's Federation, and the Parliamentary Medical Committee.

At its first meeting on 7th May, 1941, the Commission established six main committees, five dealing with more or less clearly defined branches of medical activity, and the sixth co-ordinating the work of the other committees. The subject committees are the General Practice, Special Practice, Public Health, Hospitals, and Teaching Hospitals Committees.

The five subject committees, which have met on 31 occasions in all, have considered the principles of medical organization and reorganization within their respective spheres and have submitted reports. The Co-ordination Committee has integrated these reports in one composite document which was presented to the Commission on 29th May, 1942.

Objects of reform in medical practice and provision.—The Commission has adopted for the purpose of its discussion the following broad definition of the objects of medical service in this country:—

(a) To provide a system of medical service directed towards the achievement of positive health, the prevention of disease, and the relief of sickness.

(b) To render available to every individual all necessary medical services both general and specialist, and both domiciliary and institutional.

Some criticisms of present medical services.—The diffusion of responsibility for the country's health services among a number of statutory central and local authorities is a weakness of the present administrative system. In part the explanation lies in the mode of development of the public health services. Originally established to meet the peril of cholera in 1831, these services were closely associated with public assistance and were centrally supervised or controlled, first by a Central Board of Health and later by the Local Government Board. Then the Local Government Board was succeeded by the Ministry of Health as a further expression of the policy of central integration. But the intention of Parliament in 1919 to bring the school medical service within the same ambit was frustrated by the Education Act of 1921, nor were any steps taken to transfer to the Ministry of Health the health functions of some other Government departments. Thus at the present time civil medical functions are distributed among the Ministry of Health, the Board of Education, the Home Office, the Ministry of Pensions, the Ministry of Labour, the General Post Office, and the Ministry of Supply.

The report then outlines the development of public health movements in England, Scotland

and Northern Ireland and points out the anomalies and gaps in legislation and administration and then continues

Local health authorities were developed originally to administer sanitary services and to control infectious diseases, but since the early part of the present century they have assumed functions in relation to personal health services—for example, in regard to mothers and children, and to persons suffering from tuberculosis, venereal diseases, mental disease (including mental deficiency), and orthopaedic and other conditions. The structure and practice of local authorities, however, have not been sufficiently modified to adapt them to their changing responsibilities. Further, local authorities have often developed their personal health services without adequate consultation with the profession and without consideration of other authorities, both State and voluntary, working in the same field.

The composition of local authorities is also the subject of criticism from the point of view of modern medical services. The members of local authorities are elected by the local population on the basis of local interests or political views and not necessarily for their competence to deal with the problems of modern social services. The rapid advance of medical science and the increasing complexity of medical practice have outstripped the ability of the average local councillor to make informed decisions concerning the provision and management of medical services, and too often policy is determined by local politics and personal factors.

The report points out the anomalies and defects in the hospital system and states that 'the deficiency and maldistribution of hospital accommodation, taking the country as a whole, have not been remedied', and continues

The foregoing criticisms may be summed up in the general criticism that there has been no comprehensive national health policy to guide legislative and other developments in the sphere of medical service. The distribution of executive and administrative functions among statutory bodies, both central and local, has been haphazard. There are too many central and local bodies concerned with one or another aspect of the country's health services, and too little collaboration between statutory bodies and between statutory and voluntary bodies. There has been insufficient consultation with the medical profession, both centrally and locally, on those important aspects of health administration upon which it is well fitted to advise. Where advisory machinery has been created it has rarely been utilized.

Another complaint is that economic status rather than medical need is felt to be too often the criterion of eligibility for medical service. The distribution of doctors, both general practitioners and specialists, is said to be governed more by the economics of the medical profession than by the medical needs of the various types of area. Consultant and specialist services are not always conveniently available, partly because practitioners engaged in them tend to concentrate in university centres and the large towns.

The sense of isolation is one of the chief grievances of the general practitioner. Though verbal tribute is often paid to the important place of the general practitioner in the pattern of the country's health services, in practice statutory bodies do not generally admit him to partnership with them, and even tend to widen the gap between official services and general practice.

There is another form of isolation which the general practitioner experiences. The days when a doctor armed only with his stethoscope and his drugs could offer a fairly complete medical service are gone. He

cannot now be all-sufficient. For efficient work he must have at his disposal modern facilities for diagnosis and treatment, and often these cannot be provided by a private individual or installed in a private surgery. He must also have easy and convenient access to consultant and specialist opinion, whether at hospital or elsewhere, and he must have opportunities for real collaboration with consultants. Facilities such as these are inadequate at the present time. There must also be close collaboration among local general practitioners themselves, for their different interests and experience can be of value to each other. Although this need is recognized by practitioners collaboration has not been developed as it should be.

Other criticisms offered by general practitioners relate to the conditions in which they work. There are insufficient facilities for regular post-graduate study and the development of special scientific and clinical interest. The pressure of work which may be ascribed in part to bad distribution, often leads to excessive hours of duty and insufficient holidays. Some criticisms of the present system concern finance.

Other defects result from the existence side by side of two essentially different hospital systems—the individualistic voluntary hospital depending for its continuance on voluntary enterprise and staffed by medical practitioners who in most cases receive no direct remuneration for their services and the municipal hospitals administered by local government authorities and staffed by practitioners who are paid officers of the local authorities. Many of the differences that exist between the two systems—such as the conditions of admission of patients and the opportunities offered for professional careers—are fundamental, and their continued existence is detrimental to the development of an efficient hospital service.

These are some of the deficiencies and defects which are stated with varying emphasis by the public and by doctors to exist to-day. While it is not necessary to accept them all as of equal importance or validity, it cannot be denied that there is some foundation for most of them.

DISCUSSION

Some principles.—What steps should be taken in the public interest to improve the community's medical services as a whole? Any proposals for reform must have as their object the largest possible measure of improvement in the public health. They must aim at improvement in the quantity, the quality, and the availability of all types of medical service. Doctors must be competent and have time to devote to those medical services which they undertake to give. They must have facilities for rendering them at the highest possible level of efficiency. The public must have access to all services with the maximum amount of convenience and comfort.

The reform of the medical and health services of the country should include measures for securing that each family or individual shall be under the care of a medical practitioner who shall be concerned not only with diagnosis and treatment but also with the promotion of health and the prevention of disease. This involves the integration of preventive and personal health services. It also involves radical changes in the country's administrative machinery and in the training of medical students. It assumes that the fusion of public health and other forms of practice will result in practitioners in every field working in closer contact and accord not only with one another but also with dentists, nurses, midwives, sanitary inspectors, and other auxiliaries.

While there is general agreement on the objects desired, there is difference of opinion as to the best way of achieving them.

The function of the general practitioner.—There seems to be general agreement with the view expressed in 1920 by the Consultative Council on Medical and Allied Services of the Scottish Board of Health that the organization of the national health services should be based upon the family as the normal unit and on the family doctor as the normal medical attendant

and guardian. The first essential is not institutional but personal service, such as can be rendered by a family doctor who has the continuous care of the health of the families under his charge. To him they will turn for advice and help. He will afford them such professional services as he can render personally, and will make it his duty to see that they obtain full advantage of all the further auxiliary services that may be otherwise provided.

Co-operation in general practice.—Diverse as are the views on the organization of medical services, there is general agreement that co-operation among individual general practitioners in a locality is essential to efficient practice under modern conditions, though views vary on the form of the co-operation. The principle of the organization of general practice on a group or co-operative basis is widely approved. A convenient term for the focal point of co-operation is 'health centre'. The general suggestion is that there should be available at local health centres certain facilities for diagnosis and consultation and, in appropriate areas, facilities for the work now undertaken by general practitioners at their own surgeries and for such of the work now undertaken at local authority clinics. The nature and functions of a health centre are discussed more fully later in this report.

Hospital reform.—The report outlines briefly what has been done in this respect. There is general agreement that the present unco-ordinated hospital services should give way to a unified hospital system. The organization of all hospital services on a regional basis is generally favoured.

Possible lines of development of medical services.—Division of opinion is exhibited in the types of proposals for such reform as will remove the defects and deficiencies of the present system. The three main types—namely, the improvement and development of the existing system, the whole-time salaried medical service, and the intermediate schemes—are briefly outlined below. The question of hospital reform is dealt with in a subsequent section.

Development of the existing system.—It is logical to set out first the view of those who believe that, in spite of the admitted defects and omissions of the present system, an endeavour should be made to build for the future on the existing foundations rather than to devise an entirely new structure. The best-known exponent of this view has been the British Medical Association, whose policy was described in its 'General Medical Service for the Nation'.

The scheme provides for a complete general medical service with domiciliary, institutional, maternity, consultant and specialist, and auxiliary services. It proposes the inclusion in the National Health Insurance scheme of the dependants of the present insured persons, those at present receiving domiciliary medical attendance through public assistance machinery, and other persons, with their dependants, of an economic status similar to that of the present insured persons. It is estimated that these groups constitute approximately 90 per cent of the population.

The opponents of such evolutionary development maintained that the defects of the present system are inherent and cannot be remedied except by a radical change in the structure. They say that efficient service cannot be obtained from a system where doctors compete for patients, where practice and partnership arrangements are on a business basis, and where general practices are bought and sold. The opponents of the present system further maintain that existing conditions breed suspicion and resentment and friction between doctor and doctor, and between the doctor, the hospital, and the public health authority.

A whole-time salaried medical service.—The advocates of a whole-time salaried service base their plan on the thesis that the provision of a medical service, like that of an educational service, is a function of the State, that competition in private medical practice is undesirable and should in time become unnecessary. If the objects defined by the Commission are to be fulfilled there must be provided a complete preventive and curative service, and no question of inability to pay

should deter people from obtaining all the benefits inherent in these. The service should be nationally planned and controlled but administered by regional authorities covering large areas and giving full representation to the medical profession on advisory councils, local, regional and central; and also providing elasticity and freedom from bureaucratic control in the local health units. The doctor would become a salaried officer with all the benefits which this implies. His advancement and remuneration would be related to length of service and merit and to the nature and responsibilities of the post held.

This health service would be organized locally through a system of health centres so placed and staffed as to meet the needs of the population, linked with the hospitals and all specialist services. Health centres would replace, except in remote areas, the doctors' surgeries; organize the work of practitioners and consultants and carry out the work of certain existing clinics; organize the work of the ancillary services, and carry out health education.

The opponents of a whole-time Government salaried medical service also fear the intrusion of politics, both national and local, into the field of medical service, an intrusion which they maintain would be disastrous. They hold, further, that the 'cold hand' of bureaucratic control, with the doctor acting under the orders of superior officers, whether medical or lay, would be inimical to the wise and humane administration of a personal health service.

Other objections to the whole-time salaried medical service are then outlined.

The intermediate schemes.—Some people who think that a mere extension of the National Health Insurance system would be an inadequate measure of reform are yet not prepared to go so far as to recommend a whole-time salaried medical service. They therefore suggest a service intermediate between the two which would be based primarily on part-time salaried public service with opportunities for private practice.

The majority view.—The majority view of the committees which have discussed this matter is against a whole-time salaried Government service. It is felt that some of the advocates of a whole-time salaried medical service tend to paint an unduly gloomy picture of present-day medical practice.

The report believes that most of the faults of the present services would be remedied by adaptation, augmentation, re-orientation of existing services so as to integrate them into a co-ordinated whole.

PROPOSALS

Administration.—This group of proposals is set out first as it is regarded as fundamental to the whole plan. Unless and until the main features of the structural changes find expression in legislative action, the other reforms here recommended will be denied the foundation they need. This is not to say that considerable progress cannot be achieved in a comparatively short time by interim measures.

Central administration.—A central authority should be established to be concerned solely with all the civilian medical and auxiliary services of the country. This authority may be a Government department in the usual sense or it may be a corporate body formed under Government auspices and responsible through a Minister to Parliament. It should have a medical practitioner as its chief officer. It should deal with civilian medical and ancillary health services, and the medical treatment of pensioners. These proposals for the establishment of a central authority extend to Scotland as a separate national unit. The report suggests the form that such Government departments or corporate bodies might take.

Local administration.—The local administrative body would be concerned with administration within the framework of the policy laid down at the centre. It is important to emphasize that the formation of policy should be the responsibility of the central authority. The local authority should be purely administrative.

The system under which local authorities administer in detail a broad national policy decided by the central Government is deeply embedded in the social fabric of this country. There is, however, general agreement that many of the existing local units are too small or too poor, or both, to administer such services efficiently. The population of such areas should as a rule be not less than 500,000.

The report then discusses the organization of work under regional authorities or regional councils, and then goes on

Group medicine and health centres.—Some of the difficulties that beset the general practitioner to-day arise from the rapid advance of medical science and the increasing complexity of medical practice. Others are due to the isolation of the general practitioner from consultant and specialist services, from hospital services, from public health services, from administration, and from his own colleagues; to the failure of public authorities adequately to recognize the value of the general practitioner; and to the continuance of traditional individualism into an age where division of labour and co-operation are essential factors in social service.

Greater efficiency and economy would be secured and less expense incurred if groups of practitioners would co-operate to conduct a single centre at which all of them would see their own patients and share equipment and the services of secretarial, domestic, and dispensing staff. The value of the practitioner to his patients would gain immeasurably from his close and constant contact with his colleagues.

Group or co-operative general practice is desirable, though some variation of the organization would be necessary in sparsely populated areas. In the following paragraphs a scheme for group practice is outlined which it is believed would be workable in many areas and which would go far to meet the defects of the present system.

The report discusses several different ways in which the health centres might be organized.

Model health centre.—The paragraphs that follow contain suggestions for a standard form of health centre that may be adapted to suit local conditions.

Provision of centre.—The health centre being an official part of a regional authority's comprehensive medical service, the building and equipment would be provided or approved by the authority.

Clientele.—It is recommended that a State scheme of medical service should be provided for all persons with incomes within the current National Health Insurance limits and for their dependants, in effect for about 90 per cent of the population. The general medical care of these persons would be undertaken by general practitioners of their choice either at the centre or in their own homes. Persons outside the scheme would attend at the centre or at the practitioner's private residence or would be visited in their own homes as mutually arranged.

Service available.—General practitioners would attend at the centre at hours convenient for their patients and would pay domiciliary visits from the centre. They would undertake ante-natal, natal, and post-natal work; they would take part in infant and child welfare and the school medical service; they would arrange consultations with specialists, some of whom might attend at the centre; and they should be associated with the local hospitals. The work of the centre would be preventive and educational, as well as curative. Midwifery, nursing, and auxiliary services would be available at or through the centre, midwives, health visitors, and district nurses working from the centre. The centre should have ready access to an x-ray and a pathological department at the centre or elsewhere, these departments being under proper specialist supervision. Dispensing might continue on the present National Health Insurance lines or be arranged at the centre, but in any case a dispensary service for drugs, etc., required by the practitioner for immediate

application would be conducted at the centre. A communal service would be maintained for record-keeping and secretarial work.

Accommodation.—The accommodation could include : (i) A consulting room for each doctor working at the centre at any one time. (ii) Waiting rooms. There might be several moderate-sized waiting rooms, which would be used in common and not allocated to particular practitioners. (iii) A small theatre for minor surgery within the competence of a general practitioner. (iv) A pathological room for simple diagnostic investigation. There would be accommodation for a resident caretaker and for secretarial work and records.

Size and area.—The area covered by the centre would not be too large, partly in order that patients should not be required to travel far. The number of practitioners co-operating to provide the service would depend upon the size and nature of the area served, but it would normally be from 10 to 12 in urban areas and 6 to 8 in mixed areas.

Local authority services.—The medical staff as a whole would assume responsibility for the ante-natal, post-natal, infant welfare, and school medical work which is at present rendered by the medical staff of local authorities.

Work in tuberculosis, venereal diseases, mental deficiency orthopaedics, child guidance, and in other such specialized branches would not be undertaken at the centre or by the centre staff but at special clinics with specialist staffs.

Conditions of service of medical staff.—The terms and conditions of service for both principals and assistants in respect of persons covered by the scheme would be on a nationally agreed basis.

The report discusses the staffing and remuneration, and administration of these health centres.

Rural areas.—The form of health centre suggested above is primarily applicable to urban and mixed areas, but its principles are also applicable, with suitable variations, to rural areas.

The report advocates the immediate adoption of some measures outlined in the report with a view to the adoption of the entire scheme at a later date.

Hospital and specialist services.—An important paragraph of this section of the report is as follows :—

In a regional scheme all hospital provision and the higher administration of the hospital services would be the province of the Regional Council or Authority. The latter would not interfere with the internal organization of individual hospitals, but the general conditions in all the hospitals should be similar. It is undesirable that in a unified scheme the important differences that prevail to-day between voluntary and council hospitals should persist.

The report stresses that the conditions of admission to hospitals should be on the same basis. The report then discusses at length the staffing of hospitals and suggests that this should be supervised by the regional authority and that the distinctions between voluntary and council hospitals should be removed. It suggests that appointments be of three types, whole-time salaried with no private practice, whole-time salaried with limited private practice within the hospital, and part-time salaried with private practice in or outside the hospital.

The report discusses also the following subjects : Consultant services for smaller hospitals, remuneration of staff, selection of staff, arrangements for staff to visit other hospitals or countries, and the internal administration of the hospitals.

A special section of the report deals with teaching hospitals. Here again immediate proposals for action are made.

Another section of the report deals with specialists and consultant practice which, it is stated, 'needs re-orientation'. The report ends with a brief reference to industrial health, the importance of which is emphasized and which is to be the subject of a subsequent report.

Current Topics

Transactions of the Royal Society of Tropical Medicine and Hygiene, London

36, 123-196 (November), 1942

SPRUE, by H. S. Stannus, p. 123.

The Morphology of the Blood in Dimorphic Anæmia, by H. C. Trowell, p. 151.

Studies on Hepato-lienal Cirrhosis in Eastern Mediterranean Countries, by R. Reitler and S. Blesch, p. 177.

Relapsing Fever in Abyssinia, by M. J. Souttar, p. 189.

The Efficiency of Headgear as Insulation against Radiation, by J. Glover, p. 195.

(We quote below the authors' own summaries of the first four papers.)

SPRUE

A. Criticisms are offered upon theories previously enunciated concerning the causation of sprue and upon some of the observations upon which they are founded.

B. An attempt is made to suggest the lines along which a solution of the problem may lie.

C. Evidence is adduced in favour of a theory based upon the 'partition' hypothesis which predicates for unsplit (neutral) fat and for fatty acids a different mode of absorption from the intestine, a different route after absorption, a different composition during trans-

port, a different destination and a different rôle in the bodily metabolism.

D. The theory now tentatively put forward regarding the pathogeny of sprue enlists the following considerations :—

(1) The deficient absorption of fat is limited primarily to loss of power to absorb the fatty acid moiety and cholesterol.

(2) There is no loss of power to absorb neutral fat (glyceride) but there is a deficiency of neutral fat absorption due, secondarily, to non-absorption of fatty acid.

(3) There is also a primary loss of power to absorb glucose which results in a low flat oral blood sugar tolerance curve, glucose no longer being selectively absorbed by an active process but only by diffusion.

(4) The same is true of glycerol formed by the splitting of neutral fat.

(5) The loss of power to absorb fatty acid, glycerol and glucose is due probably to failure of phosphorylation. They are all substances, as opposed to many others, which require to be phosphorylated on absorption by the intestinal mucosa.

(6) Neutral fat is normally absorbed as a finely dispersed emulsion and does not require to be phosphorylated. Failure of absorption is secondary to non-absorption of fatty acid.

(7) Fructose (laevulose) is normally absorbed without phosphorylation and utilized by the sprue patient as by the normal subject.

(8) Loss of calcium to the body is due to 'fixation' by fatty acid in the bowel with the formation of insoluble soaps.

(9) Loss of phosphorus is due to defect in phospholipid formation resulting from failure of phosphorylation.

(10) The effect of the mass of unabsorbed fatty acid and collection of gas due to the fermentation of unabsorbed glucose upon the small bowel is to produce intestinal delay in the small bowel and a passive distension, together with the other signs commonly demonstrated by radiographic examination.

(11) The primary failure in sprue, as above stated, is one of phosphorylation, not due, as suggested by Verzar, to lack of adrenal hormonal control, but the result of defective enzymic action.

(12) The enzyme or enzymes which catalyse phosphorylation—the 'carriers' of phosphoric acid—probably have as the active part of the molecule co-enzymes embodying some member or members (identified or unidentified) of the vitamin-B₂ complex—all present in crude liver extracts. These may include riboflavin, nicotinic acid and pyridoxin. It may be remembered that choline is sometimes now included in the B₂ complex.

(13) Whether the same enzyme catalyses the phosphorylation of all of the several substances is uncertain.

(14) Since normally the phospholipids (lecithins) synthesized by the intestinal mucosa from fatty acid, glycerol, phosphoric acid and choline contain unsaturated fatty acids it is possible that desaturation occurs at the same time as phospholipid synthesis. In view of the close association of pyridoxin with unsaturated fatty acids, it seems possible it may here be at fault in sprue.

(15) The nature of the fatty acids in the diet may be a factor in determining the distribution of the disease.

(16) The loss to the body of certain phospholipids containing highly unsaturated fatty acids may be a factor in the causation of the anaemia in sprue and of other nutritional anemias.

(17) There are no pathological changes in sprue.

There is no secretory failure and no failure of absorption except that resulting from defect in phosphorylation.

(18) Sprue is properly placed among the diseases of malnutrition.

THE MORPHOLOGY OF THE BLOOD IN DIMORPHIC ANAEMIA

1. The modern approach to anaemia consists in stressing the deficiency aspect of anaemia even when this deficiency is occasioned by, or increased in, a certain disease. Anaemia is seldom regarded as entirely secondary to disease unless this disease causes severe haemolysis.

2. This outlook has not been applied to the classification of anaemia in the tropics, where anaemia is regarded as due almost exclusively to the presence of tropical diseases.

3. Most cases of anaemia in Uganda natives show evidence of a dual deficiency of iron and of that present in nutritional macrocytic anaemia.

4. It is suggested that this should be called dimorphic anaemia.

5. One hundred and seventy-four cases of anaemia in Uganda natives were examined by estimation of M.C.V., M.C.H.C., peripheral blood counts, sternal puncture, test meal, van den Bergh reaction and the reticulocyte response to iron and to liver.

6. One hundred of these cases appeared to be cases of dimorphic anaemia.

7. The commonest cause of severe iron deficiency in dimorphic anaemia appeared to have been a heavy hookworm load and a diet deficient in iron.

8. The commonest cause of the nutritional macrocytic anaemia type of deficiency appeared to have been due to a diet poor in meat and possibly in green vegetables.

9. The sternal dry smear has been examined in 162 of these 174 cases and in some 145 other cases of anaemia and the megaloblastic tendencies in erythropoiesis in nutritional macrocytic anaemia and the hypochromic regeneration in iron-deficiency anaemia are described in detail and compared with normal erythropoiesis studied in eight normal Africans.

10. In dimorphic anaemia all three types of erythropoiesis can usually be detected, hypochromic, megaloblastic and normoblastic, the latter, however, usually predominating.

11. The morphology of the peripheral blood is described. Hypochromic cells are concentrated in the central parts of the smear whereas orthochromic macrocytes are collected at the tail. This is usually so characteristic that a diagnosis of dimorphic anaemia can be made at once in most cases.

12. These views must not be construed to deny the fact that in well-fed persons malaria produces a pure haemolytic anaemia and hookworms a pure post-haemorrhagic iron-deficiency anaemia, neither of which comes under the category of dimorphic anaemia.

STUDIES ON HEPATO-LIENAL CIRRHOSIS IN EASTERN MEDITERRANEAN COUNTRIES

1. Various strains of *Staphylococcus pyogenes* were cultured from the blood of patients suffering from Mediterranean hepato-lienal fibrosis.

2. Intravenous injections of one of these strains caused, in rabbits, pathological changes in the liver similar to the changes found in human hepato-lienal fibrosis.

3. The close association of the disease with intestinal parasitic infestation and nutritional deficiencies is noted.

4. It is supposed that the staphylococcus gains entrance to the blood stream through the minute injuries of the intestinal mucosa caused by the parasites and the development of the disease is aided by the nutritional deficiencies.

RELAPSING FEVER IN ABYSSINIA

1. Twenty-eight bacteriologically confirmed cases of relapsing fever are reviewed occurring in Gold Coast soldiers in Abyssinia.

2. There were nine fatal cases, six of them occurring on the second day after admission.

3. It is suggested that greater altitude tends to a higher mortality.

4. It is suggested that the treatment of choice is to give intravenous arsenicals to all cases however jaundiced.

5. Twelve other probable cases are mentioned, though spirochaetes were never found in blood films.

Indian Journal of Medical Research

30, October 1942, pp. 481-644

COMPARATIVE Study of Human Immunization with Two and Three Doses of Tetanus Toxoid, by D. C. Lahiri, p. 481.

Post Kala-azar Infection of the Skin by *Leishmania donovani*, by P. N. Brahmachari, p. 485.

* Vitamin C in Germinating Grains, by Kamala Bhagvat and K. K. P. N. Rao, p. 493.

* Vitamin-C Content of Dry Bengal Gram, by Kamala Bhagvat and K. K. P. N. Rao, p. 505.

* Vitamin-C Content of Tender Walnut, by S. Ranganathan, p. 513.

* Vitamin-C Content of Some Dehydrated Vegetables and Fruits, and of Fruit Juice Preparations, by S. Ranganathan, p. 517.

* The Effect of Dehydration and Reconstitution on the Carotene Content of Certain Vegetables, by N. S. Sekhon, p. 529.

* The Application of the Cyanogen Bromide Test to a Study of the Metabolism of Nicotinic Acid in Rabbits, by M. Swaminathan, p. 537.

Vitamin-A Content of Liver Oils of Some Indian *Elasmobranchs*, by P. N. Sarangdhar, p. 553.

- * Dental Caries in Children in Madras City in Relation to Economic and Nutritional Status, by K. L. Shourie, p. 561.
 - * Investigations into the Biological Value of Milk Proteins, Part II, by the Balance-Sheet Method, by K. Mitra and H. C. Mittra, p. 575.
 - * A Diet Survey of Nizamabad District in H. E. H. the Nizam's Dominions, by M. B. Daver and S. S. Ahmed, p. 581.
 - * Influence of the Anterior Lobe of the Pituitary Gland on Calcium Metabolism, Part I, Calcium Balance, by K. N. Krishnan, p. 589.
 - * On Serum Phosphatase, Part I, The Serum Phosphatase in Pulmonary Tuberculosis and the Effect of Ingestion of Vitamin C Upon It, by M. N. Rudra and S. K. Roy, p. 603.
 - * On the Suitability of the Guinea-pig Method of Digitalis Assay in India, by B. C. Bose and B. Mukerji, p. 611.
 - Partition of Phosphorus in Mammalian Brains, by N. L. Lahiry, P. R. Venkataraman, C. P. Anantakrishnan and N. N. De, p. 619.
 - * Observations on the Behaviour of Pulmonary Vessels in the Isolated Perfused Rat Lungs, by A. S. Sinha, p. 623.
 - * The Interaction between Ions Drugs and Electrical Stimulation as Indicated by Inhibition in Unstriated Muscle, by I. Singh, p. 629.
- (Of papers marked * the author's summary is given here.)

VITAMIN C IN GERMINATING GRAINS

1. A study has been made of the effect of germination, cooking and drying on the vitamin-C content of certain pulses and cereals.
2. In the dry state, most of the grains contained small or negligible amounts of vitamin C. Bengal gram, however, was found to contain from 6 mg. to 20 mg. and green gram 8 mg. to 10 mg. per cent.
3. Soaking had little effect on vitamin-C content.
4. Vitamin C is rapidly formed when germination begins. The concentration reaches its maximum in 30 to 48 hours, after which it remains constant for 3 to 4 days. Green gram gave the highest vitamin-C titre after germination.
5. Vitamin C is found both in the cotyledon and the sprout, the percentage present in the latter increasing, and that present in the former decreasing, as germination proceeds.
6. Considerable loss of vitamin C takes place when germinated pulses are cooked. The drying of germinated pulses also leads to loss, and the vitamin C which remains after drying is not suitable on storage.

VITAMIN-C CONTENT OF DRY BENGAL GRAM

1. Dry samples of Bengal gram were found to contain significant amounts of vitamin C which were sufficient to promote good growth in guinea-pigs when fed at 32 and 50 per cent levels of intake respectively. This observation may have a bearing on the apparently low incidence of severe scurvy in India.
2. Evidence has been brought forward to show the presence in pulses of an alkali-stable growth-promoting factor for guinea-pigs.

VITAMIN-C CONTENT OF TENDER WALNUT

1. Immature walnuts are a rich source of vitamin C, containing nearly 15 milligrams per gramme of fresh material. This is present mainly in the pulp. As the fruit ripens and the nut is formed, the vitamin disappears.

2. The use of tender walnuts as a source of vitamin C does not appear to be very practicable.

THE VITAMIN-C CONTENT OF SOME DEHYDRATED VEGETABLES AND FRUITS, AND OF FRUIT JUICE PREPARATIONS

1. An investigation of the effect of dehydration on the vitamin-C content of various vegetables and fruits is reported.
2. The dehydration of vegetables in general destroys most of the vitamin C present in the fresh material. Certain vegetables, however, retain vitamin C in appreciable quantities, after dehydration.

3. The vitamin-C content of dehydrated vegetables falls rapidly on storage.

4. Reconstitution and cooking lead to further losses of vitamin remaining in dehydrated vegetables. Much of the vitamin C that survives passes into the cooking water.

5. Amla fruit after dehydration remains rich in vitamin C, which is *relatively* stable in amla powder and tablets. Steady loss, however, occurs on storage. The presence of tannins in amla does not interfere with the estimation of vitamin C.

6. It was not found possible to prepare a stable powder rich in vitamin C from country guava. Similar experiments with cashew apple, papaya and pineapple were also unsuccessful.

7. Fruit juice and fruit juice concentrates cannot be recommended as anti-scorbutics, the vitamin in such preparations being very unstable.

THE EFFECT OF DEHYDRATION AND RECONSTITUTION ON THE CAROTENE CONTENT OF CERTAIN VEGETABLES

1. The effect of dehydration and reconstitution on the carotene content of various vegetables has been studied.

2. Losses on dehydration are not serious, ranging from almost *nil* to about 15 per cent. The loss in a sample of potato subjected to steam-blanching before dehydration was considerably greater. Reconstitution by cooking leads to losses ranging from almost *nil* to 20 per cent.

3. The carotene content of dehydrated vegetables appears to be reasonably stable on storage.

THE APPLICATION OF THE CYANOGEN BROMIDE TEST TO A STUDY OF THE METABOLISM OF NICOTINIC ACID IN RABBITS

1. An investigation of the cyanogen bromide method as applied to urine has been made. Special attention has been paid to the effect of nicotinic-acid values of using various decolorizing agents, the presence of residual colour and the use of different aromatic amines under different conditions. It has been shown that consistent results can be obtained by carrying out the colour reaction in a neutral aqueous medium using aqueous aniline and the use of different decolorizing agents and the presence of residual colour does not affect the values under such conditions.

2. Nicotinic acid balance experiments were carried out on two groups of rabbits. Both groups were fed on a diet low in nicotinic acid (70 per cent per 100 g.) for a period of 10 weeks. The animals in the second group received in addition 3 mg. of nicotinic acid daily.

3. The average daily intake of nicotinic acid in the animals on the unsupplemented diet was about 97 μ g., while the daily average urinary and faecal excretion of nicotinic acid was 147 μ g. and 135 μ g., respectively, the excretion of trigonelline being 86 μ g. and 83 μ g. The total excretion was 4 to 5 times the intake. The animals which received extra nicotinic acid excreted about 15 to 20 per cent of the intake in the urine, the faecal excretion being approximately similar in both groups.

4. There was no appreciable difference in the nicotinic-acid content of the liver and muscle of the animals fed on the supplemented and unsupplemented diets. All the animals remained in good health and put on weight, irrespective of the nicotinic-acid intake.

DENTAL CARIES IN CHILDREN IN MADRAS CITY IN RELATION TO ECONOMIC AND NUTRITIONAL STATUS

1. The incidence of dental caries among 1,886 children in Madras city has been investigated. The percentage free from caries was 39.8.

2. Economic status had no influence on the caries incidence.

3. Children with deficiency diseases did not show more caries than other children.

INVESTIGATIONS INTO THE BIOLOGICAL VALUE OF MILK PROTEINS

- The digestibility coefficient and biological value of the proteins of buffalo, cow and goat milks were determined by balance-sheet method at 10 and 15 per

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cent levels of intake. No difference in digestibility was observed between 10 and 15 per cent levels of protein intake; in the case of all the three milks the proteins of cow milk gave the highest figure for digestibility, with those of goat and buffalo milk closely following in that order. Lower figures for biological value were obtained at the 15 per cent level of intake than at the 10 per cent level in the case of all the three milks. At the 10 per cent level cow milk gave the highest figure and no appreciable difference between the proteins of the other two kinds of milk was observed. At the 15 per cent level, the difference between the three were almost negligible.

A DIET SURVEY OF NIZAMABAD DISTRICT IN H. E. H. THE NIZAM'S DOMINIONS

1. A diet survey has been carried out in the Nizamabad district of Hyderabad. The survey included 147 families. The families were divided into six income groups.

2. Intake of calories was satisfactory in all groups; but the diets were generally deficient as regards their contents of animal protein, fat, calcium and vitamins A and C. The quality of diet improved with increasing income.

3. The incidence of xerophthalmia, evidence of vitamin-A deficiency, was high.

INFLUENCE OF THE ANTERIOR LOBE OF THE PITUITARY GLAND ON CALCIUM METABOLISM

1. The effects of the growth hormone of the anterior pituitary on calcium metabolism were investigated. The preparation used was 'Antuitrin growth' made by Parke, Davis & Co.

2. Calcium-balance experiments, using litter-mate controls of the same sex, were carried out on 32 albino rats (15 experimental and 17 control) and 11 guinea-pigs (6 experimental and 5 control) for periods ranging from 7 to 18 days. Daily intraperitoneal injections of 'Antuitrin growth' were given to experimental animals and re-distilled water to controls. The calcium content of the food, faeces and urine was estimated in all cases.

3. In all the experimental rats, with the exception of one, the calcium retention in the treated animal was considerably more than that in the control, the average value being 50 per cent above. In 4 out of 6 experiments on guinea-pigs the average value was 27 per cent above that of the control. The two guinea-pigs that did not give such a response lost weight in the course of the experiment.

4. There appears to be a general tendency for calcium retention to diminish with age in both treated and control rats. On the other hand, the excess retention percentage (the excess calcium retained by the treated animal expressed as a percentage of the amount retained by the control) tends to increase with age, within the age limits (57 and 218 days) of the albino rats used in this work.

5. The faecal calcium was significantly low in the treated animals as compared with the respective controls. The urinary calcium did not show any marked or constant differences.

6. The duration of injections within the limits of 7 and 18 days, sex differences, and the variations in the daily calcium intake, do not appear to have influenced calcium retention to any appreciable extent.

ON SERUM PHOSPHATASE. PART I. THE SERUM PHOSPHATASE IN PULMONARY TUBERCULOSIS AND THE EFFECT OF INGESTION OF VITAMIN C UPON IT

Serum phosphatase in pulmonary tuberculosis is generally higher than of normals.

Oral administration of large doses of natural vitamin C lowers the serum phosphatase of pulmonary tuberculosis patients.

ON THE SUITABILITY OF THE GUINEA-PIG METHOD OF DIGITALIS ASSAY IN INDIA

1. A simple method for the assay of digitalis in guinea-pigs has been described. The m.l.d. of International Standard digitalis tincture in a series of 30 guinea-pigs is found to be $9.07 \text{ c.c.} \pm 0.381$. From the

dose-mortality curve and the frequency distribution chart it appears that the method gives very dependable results.

2. In view of the easy availability, cheapness and the possibility of breeding guinea-pigs in all biological laboratories, the method should be suitable for routine laboratory examination of samples of tincture digitalis.

OBSERVATIONS ON THE BEHAVIOUR OF PULMONARY VESSELS IN THE ISOLATED PERFUSED RAT LUNGS

1. Electrical stimulation of the stellate ganglion or injection of adrenaline caused vasoconstriction and the effect was abolished by previous injection of ergotamine.

2. Electrical stimulation of the vagi had very little vasoconstrictor effect.

3. Injection of acetylcholine also produced vasoconstriction which effect was abolished by previous injection of atropine.

THE INTERACTION BETWEEN IONS DRUGS AND ELECTRICAL STIMULATION AS INDICATED BY INHIBITION IN UNSTRIATED MUSCLE

1. Inhibition is well marked in the guinea-pig uterus. Three agencies produce inhibition: (1) chemical substances, (2) electric current, and (3) increase in osmotic pressure, that is, ions within the muscle fibres. Just as the contraction produced by electric current is antagonistic to that produced by potassium, so also are the inhibitions produced by these agencies. Increase in osmotic pressure produces most of the phenomena produced by electric current. Alternating current produces two kinds of contraction as well as inhibition.

2. Plain muscle exhibits two kinds of tone, one due to slow relaxation and the other to the contraction produced by chloride. The action of sodium and chloride in the saline is antagonistic.

3. There are two kinds of spontaneous contractions, one due to alternate contractions and the other to alternate relaxation.

Penicillin Purified

(From the *Lancet*, Vol. II, 15th August, 1942, p. 189)

In the last two years Chain, Florey and their colleagues in Oxford demonstrated that a partially purified preparation of penicillin, a substance first produced from the mould *Penicillium notatum* by Fleming in 1929, possesses remarkable antibacterial activity against certain organisms and with its low toxicity has therapeutic possibilities. The penicillin preparation first used for therapeutic trials on man inhibited the growth of a number of Gram-positive bacteria at a dilution of 1:1,000,000. Yet it could be injected intravenously into mice in substantial doses without producing ill effects and could be successfully given by the same route in the treatment of bacterial infections in man. A considerable further purification of penicillin has now been reported by Abraham and Chain and the biological properties of the new product have been studied by Florey and Jennings. Its antibacterial activity is much greater than that previously obtained, the new preparation inhibiting the growth of staphylococci completely at the astonishing dilution of 1:25,000,000 and partially at a dilution of 1:160,000,000. Other Gram-positive bacteria, though not tested with the purest penicillin, which is scarce, are also inhibited at high dilutions. As Fleming showed, the Gram-negative organisms are less sensitive to penicillin than the Gram-positive ones. However, a preparation of penicillin only half as pure as the best obtained has been found to inhibit the growth of *Salmonella typhi* and *S. gaertneri* at a dilution of 1:30,000 and to have some effect at 1:120,000. Toxicity might have been expected to increase with antibacterial activity, but in fact the toxicity of the highly purified preparation is less than that of the earlier partially purified ones. A dose of 20 mg. of a penicillin preparation with half the antibacterial activity of the purest obtained had no apparent effect when injected intravenously into a 20-gramme mouse. This is a dose of at least 5,000 'Oxford units', and the effective therapeutic dose used in experiments on

mice was 5-10 units subcutaneously at three-hourly intervals. These figures give some idea of the great latitude between an effective therapeutic dose and one which a mouse will tolerate without toxic symptoms. A dose of 10,000 units in the form of a much cruder preparation given to man produced well-marked bacterial inhibition in his blood for at least an hour. Other evidence of low toxicity was that human polymorph leucocytes survived for an hour in a 1 per cent solution of purified material. In view of the very low toxicity of penicillin it may be possible to maintain concentrations in the tissues which will bring at least some of the Gram-negative organisms within its therapeutic reach.

Purified penicillin is a chemotherapeutic agent even more remarkable than the studies of the partially purified product foreshadowed. It is almost equally active against many Gram-positive organisms. It is many hundred times as active as the sulphonamides and at the same time less toxic than the least toxic of those drugs. Its antibacterial activity is not affected by tissue constituents, or within wide limits by the number of bacteria present. It has been shown to be active against sulphonamide-resistant streptococci, a property which promises to be of great value. Lately a number of antibacterial substances of various chemical constitutions have been isolated from fungi and bacteria (gramicidin and tyrocidin, actinomycin, citrinin, penicillic acid, streptothricin, gliotoxin, proactinomycin). The available evidence suggests that these substances will prove to be many times more toxic than penicillin and it remains to be seen whether any of them will stand the test as clinical chemotherapeutic agents.

Though penicillin has been purified to a high degree Abraham and Chain have not yet obtained it in a crystalline form, and it is therefore not certain that their purest preparation possesses the highest possible degree of purity. From the analytical figures of the purest penicillin preparation formulae such as $C_{24}H_{34}O_{10}N_2Ba$ and $C_{24}H_{32}O_{10}N_2Ba$ have been suggested. The nitrogen content of penicillin is remarkable since nearly all substances hitherto isolated from fungi have been nitrogen-free. The tentative formulae of penicillin, with data obtained by spectrophotometric analysis, suggest that several condensed hydroaromatic ring systems are present in the molecule. Obviously penicillin is a complex molecule, and its instability towards acids, alkalis, heavy metals and many other chemical reagents makes the task of elucidating its chemical structure more than usually difficult, so that the prospect of synthesis still seems remote. For the time being at least it will be necessary to rely on production by the mould, but in view of its potentialities methods for producing penicillin on a large scale should be developed as quickly as possible.

Utility First-Aid

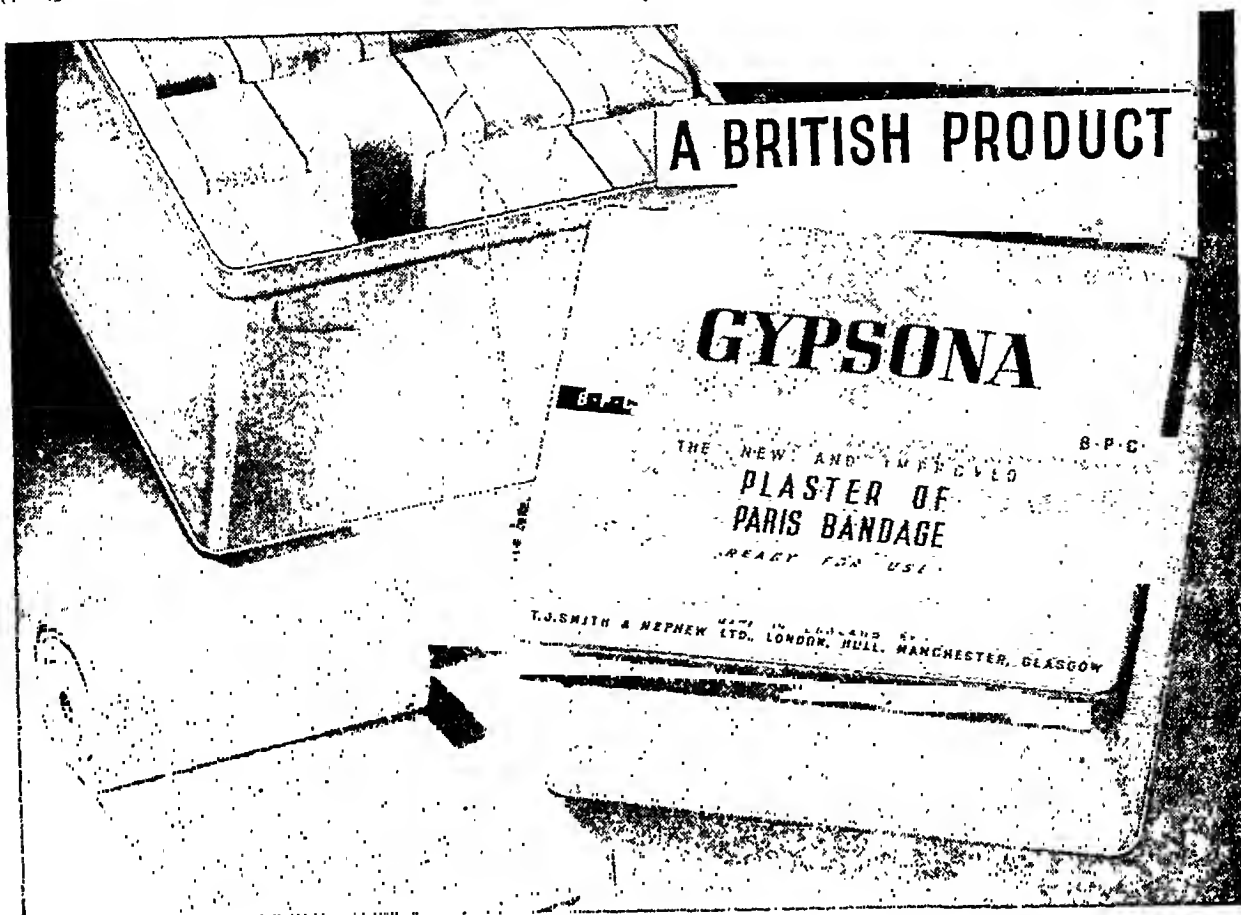
(From the *Lancet*, Vol. II, 22nd August, 1942, p. 221)

THE long-established methods of first-aid taught by the St. John and St. Andrew Ambulance Associations and the British Red Cross remain fundamentally sound, but they have now to be adjusted to meet the conditions of aerial warfare. Trueta laid down, at Barcelona, the principle that in a blitz casualties must be got to hospital as soon as possible and with the minimum of handling. To meet this new demand for simplicity and speed, methods of treatment and terminology have alike been modified. Booklets setting out the new point of view have been written by members of first-aid and stretcher parties experienced in raids. Lectures have been given to the WVS on immediate aid. Cowell has published a five-lecture course for the Home Guard on essential first-aid. At a recent course for Home Guard medical officers, H. A. Harris insisted that in the teaching of first-aid all frills and trimmings must be cut out in favour of bare essentials. A Home Guard battalion has issued its members with a folder the size of three luggage labels which details the minima of assistance, and provides a casualty label should the man be wounded. Another folder designed by Keogh sets out

in a few words and pictures what every soldier must know about first-aid. In each of the twelve Home Security regions of the country there is a regional training school, originally started for rescue parties, and later expanded to include first-aiders. Leaders of rescue, first-aid and stretcher parties now go for intensive training to these schools, so that they may return and pass on the information to their squads. Some of the schools are run by the local authorities; some are the responsibility of the regional administration.

Details vary in the different training centres, but the principles of the new utility first-aid are accepted in all. Thus all are taught that the man who first reaches a casualty should protect him as far as possible from any immediate source of danger such as moving machinery, electric cables or masonry which is threatening to fall. The first step in direct treatment is to stop bleeding by dry dressings and firm bandaging. Experience has shown that tourniquets are seldom required and it is a relief that the Samway tourniquet, first issued, has now been withdrawn. Most of the new writers agree that a tourniquet should only be used for an injury amputation. Even pressure points are given less prominence than they were. The next essential is to see that the air-passages are clear; rubble and dust must be removed from the mouth and artificial respiration given if necessary, especially if there is reason to suspect coal-gas poisoning. The methods suggested are Schafer's, Sylvester's, the rocking method and the direct method. Cleansing of wounds has to be omitted, because it is usually impossible at the site of the incident, and in any case wastes time. Splinting has been reduced to a minimum, which again saves time and lessens handling. Application of splints in the dark is a stiff ordeal even for a skilled first-aid and certainly for the patient. The patient's suffering—and therefore his shock—will be less if a broken arm is simply tied to the trunk with broad bandages, or if a fracture of the lower limb is treated by placing a rolled blanket between the legs and tying them together. The exception is a fracture of the patella, which should always be splinted. First-aid for burns now consists in covering them with a dry dressing and speeding the patient to hospital. Blanketing should be carefully taught—the Wanstead method is now universal—and first-aiders should be well drilled in lifting casualties gently on to stretchers and in loading and unloading ambulances. 'Careless handling may lose life' is a good motto. The danger period is between the time of injury and rescue and of arrival at hospital; the good first-aid will be out to make this interval as short as possible.

When many casualties have to be dealt with at one incident the worst must have priority in first-aid and transport: thus the first-aid must be able to recognize both the nature of the injury and its gravity. The concept is new, and is not touched in any of the standard manuals, but it must be taught and well taught. Thus, while teaching must be intensely practical, there must be a clear understanding of underlying principles, particularly among leaders of parties, for they not only have the responsibility of training others but must themselves be capable of quick decision in the more difficult cases. Doctors must take full part in instruction, to make certain that the standard is kept at a safe and efficient level. This cannot be left entirely to lay instructors, however keen. Sense of proportion about cases and treatment can only be acquired through medical training and experience. Shock provides a good example of the difficulty: it is an exceptional candidate for a first-aid certificate who has an intelligent grasp of this condition, even from his own necessarily limited point of view. Everyone should know the essentials of what might be called immediate help. 'First-aid' has its field and practice defined by usage, and it is to bring out the difference that such terms as 'essential aid' and 'blitz aid' have been used. The standard doctrines have not been upset, only modified; first principles remain unchanged and a sound grasp of them enables well-taught first-aiders to meet emergencies with that intelligence which rule-of-thumb methods can never confer.



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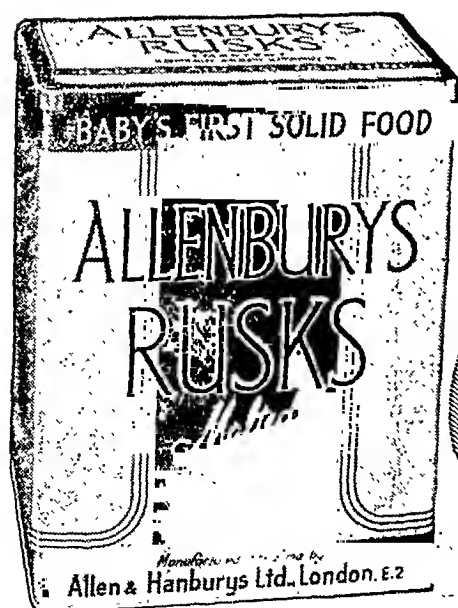
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Tannic Acid, Burns, and the Liver

(From the *British Medical Journal*, Vol. II,
12th December, 1942, p. 703)

THE tannic acid treatment of burns has by many been criticized and by some condemned on account of its local effects, especially when used on the hands and face. Its most violent critics, however, seldom disputed its value as a life-saving measure in extensive burns of the trunks and limbs, although convincing statistical evidence of its superiority over other methods has not been produced. Now comes evidence from America imputing to tannic acid to toxic effect on the liver which may kill the patient. Wells, Humphrey, and Coll report 4 fatal cases of burns in which death was attributed in whole or in part to liver necrosis. Suspecting that tannic acid was to blame, they experimented on rats, and by subcutaneous injection of tannic acid produced liver necrosis similar to that found in the fatal burns—the degree of necrosis being proportionate to the dose of tannic acid. The necrosis affects the central part of the liver lobule and is identical with that described by Wilson and his co-workers as being the characteristic lesion of burn toxæmia. It would be premature to conclude that burn toxæmia is tannic acid poisoning, but that is the suggested implication, and other agents such as silver nitrate should be employed by those who hold that coagulation is a desirable part of burn therapy.

One of the advantages claimed for coagulation is control of fluid loss, and with tannic acid now suspected as a poison other methods of achieving this end assume greater interest and importance. Siler and Reid report 134 cases treated by Koch's 'primary cleansing, compression, and rest treatment of burns' and claim good results. About a third of the burns were extensive, and only 5 patients died. These workers tried to show by experiments on dogs that the method of pressure-dressing controls hæmoconcentration and loss of plasma protein, but although their results were suggestive of a beneficial effect they were not statistically significant.

A second advantage claimed for tanning is the control of infection. This end may be attained with more certainty by sulphonamides and/or other agents such as C.T.A.B. In the series reported by Siler and Reid only one patient died of sepsis and in none were sulphonamides used, but meticulous primary cleansing is an essential part of the Koch method. Although tannic acid is suspect as a poison, a comment of Wells is worthy of note, that he would be unwilling to give up a method that has proved so beneficial, even if it did cause an occasional death. But if other agents will produce an equally beneficial coagulation it would seem wise to avoid tannic acid until it has been cleared of suspicion.

Reviews

THE VITAMINS IN MEDICINE.—By Franklin Bloknell, D.M., M.R.C.P., and Frederick Prescott, M.Sc., Ph.D., A.I.C., M.R.C.S. 1942. William Heinemann (Medical Books), Limited, London. Pp. vii plus 662. Illustrated. Price, 45s.

INSIDE the dust cover the following statements are printed regarding this book: 'This is the first comprehensive English survey of the vitamins since that of the Medical Research Council in 1932, and is presented as a practical book for all who are concerned with nutrition problems and the clinical applications of the vitamins in general medicine as well as in the treatment of frank deficiency diseases.'

In the last four years many thousands of papers on the vitamins have appeared, but as they have been scattered throughout the medical and scientific journals of the world it has been almost impossible for any

but a few research workers to have a general knowledge of the whole subject.

This book gives a full account of what is known of the vitamins, special attention being paid to their physiology and rôle in human health and medicine, since more clinical use could be made of them were their mode of action, and therefore the logic of their clinical use, more widely known.

Each vitamin is considered under the headings: History, Physiology, Sources and Food Tables, Effects of Cooking, Storage, etc., Human Requirements in Health and Disease, Clinical and Biochemical Methods of Detecting Vitamin Deficiencies, and Conditions in which the vitamin has been used clinically.

There are over 120 illustrations, mostly of cases before and after treatment, which greatly add to the practical value of the book. A very full index has been compiled so that the readers can rapidly find all the information about any subject, even though several different vitamins are concerned. The bibliographies at the end of each chapter contain the titles of over 3,000 papers.

A perusal of the book will indicate that these statements are fully justified. The work presents a very thorough and accurate survey of the present knowledge of the vitamins, and of the evidence on which this knowledge is based, and this information is presented in such a way as to be of great value to the clinician as well as to the research worker. The reviewer has found the section on the history of the different vitamins particularly interesting and informative.

The difficulty about such books as this is that by the time they become available, they tend to be out of date, since knowledge of these subjects is growing so rapidly. In this book which is published in 1943, numerous references are made to work published in 1942, so that the book should not be out of date for some little time, and one expects that new editions will appear at fairly short intervals.

It is good to see workers in India frequently quoted.

The reviewer intends to keep this book on his desk and to refer to it very frequently. He would have preferred to have the list of references given in alphabetical order of the authors' names, and not in the order in which they happen to appear in the text, for he and many others will probably use these lists as a bibliography.

The paper and get-up show some signs of war economy. The printing is good.

J. L.

A TEXTBOOK OF HISTOLOGY.—By Harvey E. Jordan, A.M., Ph.D. Eighth Edition. 1940. D. Appleton-Century Company, London and New York. Pp. ix plus 690, with 609 illustrations, many coloured. Price, 35s.

To this eighth edition of this useful book, many new illustrations have been added; the chapter on blood has been entirely rewritten, and other chapters have been thoroughly revised. The chapters on histologic technique and on directions for laboratory work have been eliminated, since teachers of histology prefer to prepare and use their own laboratory outlines, and since many special books on technical methods are now available. In the previous editions of this book, the references to literature were included in the text. In the present edition this arrangement has been changed; all references are recorded as footnotes and re-assembled in a bibliographical list at the end of the book. This is a decided improvement.

The book is divided into 19 chapters. The first chapter of 29 pages deals with protoplasm, and the cell. Subsequent chapters deal with the structure of various tissues, and the microscopic anatomy of the various organs. Then follows a list of references running into 10 pages. The author has aimed at making the list moderately extensive for the benefit of those who may wish to study a particular subject in greater detail.

The book is well printed, illustrated and bound.

D.

THE PRINCIPLES AND PRACTICE OF DIPHTHERIA IMMUNIZATION.—By J. Tutor Lewis, M.D. (Lond.), D.P.H. 1941. Oxford University Press, London, Humphrey Milford. Pp. xiv plus 155. Illustrated. Price, 8s. 6d. Obtainable from The Oxford University Press, Bombay and Calcutta.

Dr. Lewis's book on diphtheria immunization gives a good guide not only to workers in diphtheria immunization but also to general practitioners in bringing home the value of immunization to their clients. Various new points of interest have been brought out. It has been shown, for example, that the Schick test does not define a fixed level of antitoxin in the blood, but that most people with less than 0.01 A.V. per c.c.m. of blood serum are Schick-positive, and some with almost no detectable antitoxin may still be Schick-negative and consequently susceptible to diphtheria. It has therefore been suggested that a prophylactic dose should be given even to a Schick-negative reactor. Schick testing in the classical manner has been thoroughly discussed, and 7th day-reading has been advocated. Moreover, in children the omission of the control test has been advised. Amongst environmental factors of immunization, latent immunization by sub-clinical infection has been regarded as probably most important. The chapters on diphtheria prophylaxis are well written and based on experimental observations. The usefulness of all diphtheria prophylactics has been discussed in a masterly way, and the superiority of A.P.T. (alum precipitated toxoid) over the rest has been established. Subsequent Schick testing after A.P.T. in order to demonstrate the development of immunity has been declared as superfluous. The maintenance of immunity is not life-long, as is generally supposed, and hence a second immunizing dose after about four years has been advocated. At least 60 per cent of the child population must be protected by immunization in order to effect a reduction in the incidence of diphtheria. Chapters on administrative considerations and propaganda constitute a very interesting study, and reveal the exhaustive nature of work done by the author. One interesting feature of the book is that there is a summary at the end of each chapter, and also a general summary of the whole book at the end. Such a procedure is of great help to a reader of the book. The book is well got up.

G. P.

A MANUAL OF PHARMACOLOGY AND ITS APPLICATIONS TO THERAPEUTICS AND TOXICOLOGY.—By Professor Tolrauld Sollmann, M.D. Sixth Edition. 1942. W. B. Saunders Company, Philadelphia and London. Pp. x plus 1298. Price, \$8.75. London price, 45s.

PROFESSOR SOLLMAN'S Pharmacology needs no introduction; ever since its first appearance in 1917 the book has been used as a standard book of reference, most dependable, instructive and elucidative, by teachers, investigators, physicians and advanced students. In the preface to the present edition, the author modestly states that the manual 'aims to furnish a rather comprehensive outline of current knowledge and conception of drug actions'. The various actions of drugs have been fully described, and we agree with the author's opinion that the actions of a drug 'should be fully realized whenever a drug is used even for a restricted purpose'. As in the previous editions, a concise and connected story of the actions and uses of a drug has been presented in ordinary type, and the experimental facts on which the actions and uses are scientifically based have been featured in smaller type, with extensive references to authors and their works. An extensive bibliography (1920-40) has been appended; for earlier work, reference may be made to the 5th edition of the book.

A notable feature of the present edition is that in the portion dealing with *materia medica* only the most important drugs have been described. The omission of a chapter on sera and vaccines from a book on pharmacology which is meant to be used by clinicians and students may not prove popular.

In a comprehensive book of this nature, covering such a wide field, it would be strange if some statements were not found which will not receive universal acceptance; for instance, one could cite the remark about the newer organic antimony compounds that 'it is doubtful whether they are materially superior' (p. 1061). A few of the very latest developments are not mentioned, e.g., sulphathiazole in plague, stilbene in kala-azar.

However, for a single-author book of this size, the faults are very few and minor. Single authorship saves the book from the contradictions often associated with multiple authorship. The book is the best of its kind in the English language, and will continue to be widely used by investigators, clinicians and advanced students who will find it always instructive and dependable.

J. C. G.

[A 'manual' (handbook) of 1300 pages!—Editor, I. M. G.]

VENEREAL DISEASES.—By E. T. Burke, D.S.O., M.B., Ch.B. (Glas.). 1940. H. K. Lewis and Company, Limited, London. Pp. xv plus 549, with 133 illustrations and 8 coloured plates. Price, 30s.

In his preface, Col. Burke says that some of his theories—such as the 'lipoid' concept of syphilis, his views on the mode of action of arsphenamine, bismuth, iodine and mercury, on the bacteriology of gonorrhœa and on the evaluation of anti-syphilitic therapy—will clash with the ideas of many venereologists. Indeed, these views, especially those on the bacteriology of gonorrhœa, appear dogmatic and heretical in the present state of our knowledge, and are not likely to be accepted until they are proved. The rest of the book will be generally accepted as a valuable contribution. The author is a distinguished venereologist with wide experience, and he has presented much valuable information. The chapters on diagnosis are particularly good, the clinical pictures are clearly drawn, and full details of treatment have been given. The coloured plates and photographs are excellent.

R. N. C.

HYGIENE FOR NURSES.—By John Guy, M.D., D.P.H. (Camb.), F.R.F.P. & S. (Glas.), F.R.C.P. (Edin.); and G. J. I. Linklater, O.B.E., M.D., D.P.H., D.T.M. & H., M.R.C.P. (Edin.). Sixth Edition. 1943. E. and S. Livingston, Edinburgh. Pp. viii plus 240. Illustrated. Price, 5s.; postage, 5d.

In spite of the number of hygiene books now on the market, this well-known book remains the most useful of its kind for nurses. The essential principles of hygiene are well set out, and shorn of unnecessary detail that tends to confuse. The section dealing with diet and metabolism is up to date, and is of additional use to the nurse taking her dietetic course.

D. E. C.

AIDS TO ANÆSTHESIA.—By V. Goldman, L.R.C.P., M.R.C.S., D.A., Major, R.A.M.C. 1941. Baillière, Tindall and Cox, London. Pp. viii plus 235, with 58 illustrations. Price, 5s.

ANÆSTHESIA has now been included amongst the subjects dealt with in the 'Aids' series of booklets. The author, an anaesthetist of note, has produced an admirable little book. Although, like the other 'Aids', it will be of more value to those with some knowledge of the subject than to the beginner, an astonishing amount of detail has been compressed into the book without making it difficult to read.

The first chapters deal with the history, anatomy, physiology, and theoretical aspects of anaesthesia. This is all done briefly but very well. To find, in an 'Aid', chapters on the history of anaesthesia and on the personalities concerned with its development is a surprising and gratifying experience.

Although it appears in the 'Aids' series, this book is certainly worthy of the attention of the experienced anaesthetist. In particular, he will find a store of very

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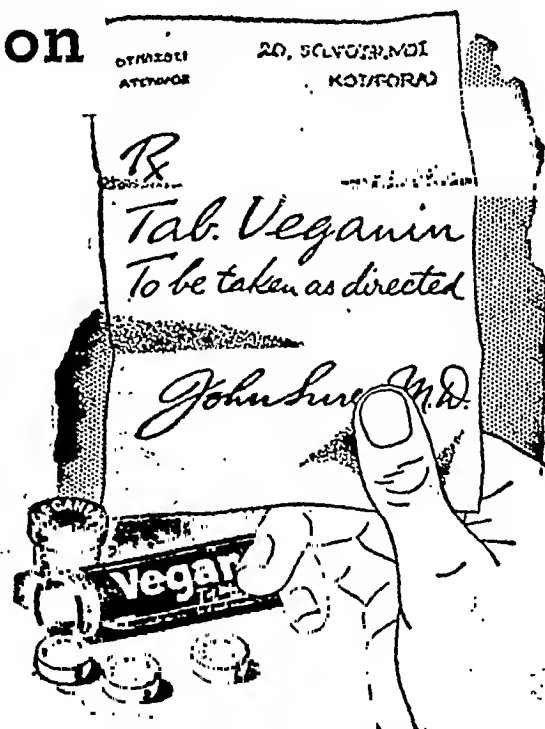
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useful information, which normally is hard to come by, in an appendix.

An invaluable revision book for those about to take their diploma.

G. R.

AIDS TO TRAY AND TROLLEY SETTING.—By Marjorie Houghton, S.R.N., S.C.M., D.N. (Lond.). Second Edition. 1942. Baillière, Tindall and Cox, London. Pp. xiii plus 210. Illustrated. Price, 4s.

I AM not surprised that a second edition of this useful little book is called for so soon. The illustrations, so ably arranged, enable nurses to visualize the requirements for each procedure, and have proved of great help in simplifying the practical work on the wards.

D. E. C.

Abstracts from Reports

SIXTEENTH ANNUAL REPORT OF THE RAMAKRISHNA MATH CHARITABLE DISPENSARY, BRODIES ROAD, MYLAPORE, MADRAS, FOR THE YEAR 1942

THE Ramakrishna Math at Madras is one of the premier institutions of the Ramakrishna Order. It maintains a charitable dispensary, which is run mainly by private financial support, and is conducted satisfactorily. During the year under report, 32,609 patients were attended in the allopathic, and 17,392 in the homoeopathic department.

The report ends with an appeal to the public to continue their sympathy and co-operation. Contributions, however small, will be thankfully received and acknowledged by the president.

THE REPORT ON THE WORKING OF HOSPITALS AND DISPENSARIES IN THE PUNJAB DURING THE YEAR 1941

THIS report deals largely with local and statistical matters of limited interest to those in other provinces. The following summary is abstracted from the introductory statement of the secretary of the Department concerned :—

The medical department of the Punjab Government showed progress in 1941 despite the war, the number of hospitals and dispensaries of all kinds rising during the year by 22 to 1,066. The subsidized practitioners' scheme under which when a medical practitioner settles in a village as the employee of a medical benefit or co-operative society, half his cost is met by Government, continued to be popular; the number of such subsidized dispensaries rose during the year by 14 to 96 (and has since increased to 110). This is not the only respect in which the people are now being encouraged to contribute towards the cost of medical treatment in order that the official provision available may be spread to greater advantage : one district board at least is now levying a small charge upon out-patients, and a similar small charge (except in the case of the obviously indigent) is shortly to be imposed in the case of all Government hospitals and dispensaries.

The number of Government medical officers of all classes increased during the year from 1,243 to 1,288. There has, however, been a considerable reduction since on account of the calls of the army, and as this is the last review of the administration of the medical department which the Punjab Government are likely to issue while the war lasts, they take the opportunity to make it known that of their 720 male medical officers 254 had at the end of 1942 joined the forces. In particular, most of the I.M.S. officers have now returned to military duty, and one only remains who is

under 50. As far as possible the vacancies caused are being filled by the re-employment of retired medical officers. A substantial number of posts, however, remains vacant, and in many parts of the province one medical officer is having to hold charge of two dispensaries.

During the year the number of in-patients and out-patients was almost exactly the same as in 1940, viz, 8,500 per day in-door and 104,000 per day out-door. As in other years, eye conditions of one kind or another head the list of diseases from which patients seeking treatment were suffering. There has been some decrease in the number of tuberculosis patients though it is doubtful whether this represents any real decrease in the incidence of the disease. A number of new tuberculosis clinics were indeed opened during the year, and others are in contemplation. Prevention (which is the important matter in the case of this disease) is of course bound up with public housing and nutrition, subjects which are receiving the attention of Government in their health department.

Service Notes

APPOINTMENTS AND TRANSFERS

THE VICEROY AND GOVERNOR-GENERAL has been pleased to make the following appointment on His Excellency's personal staff, with effect from the date stated :—

To be Honorary Surgeon

Colonel (L/Brig.) G. Covell, C.I.E., *vice* Colonel P. B. Bharucha, D.S.O., O.B.E., vacated, 21st February, 1943.

Lieutenant-Colonel R. F. D. MacGregor, C.I.E., M.C., I.M.S. (Retd.), is appointed Officer on Special Duty in the office of the Director-General, Indian Medical Service, with effect from the 1st March, 1943.

The services of Lieutenant-Colonel M. M. Cruickshank, C.I.E., are placed temporarily at the disposal of His Excellency the Commander-in-Chief, with effect from the 20th March, 1943.

Lieutenant-Colonel G. H. Mahony, I.M.S. (Retd.), is temporarily appointed as Civil Surgeon, Darjeeling, for a further period of 1 year, with effect from the 3rd February, 1943.

Lieutenant-Colonel K. S. Thakur, I.M.S. (Retd.), is temporarily re-employed as Civil Surgeon, 24-Parganas, for a further period of 1 year, with effect from the 2nd April, 1943.

Lieutenant-Colonel D. R. Thomas, O.B.E., assumed charge of the office of Chemical Examiner to Government, Punjab, on the afternoon of the 22nd April, 1943. He will also work as Chief Medical Officer, Air Raid Precautions, Punjab, in addition to his own duties as Chemical Examiner.

Major Sir Clutha MacKenzie is appointed Officer on Special Duty in the office of Director-General, Indian Medical Service, with effect from the 14th January, 1943.

The services of Major A. N. Chopra are replaced at the disposal of the Government of the Central Provinces and Berar, with effect from the 1st March, 1943.

On transfer from the Medical School, Amritsar, Major S. M. K. Mallick assumed charge of the office of Deputy Inspector-General of Civil Hospitals, Punjab, on the forenoon of the 7th April, 1943.

Major H. B. Wright is appointed as Deputy Assistant Director-General (Medical Stores), Calcutta, with effect from the afternoon of 3rd April, 1943, *vice* Major W. T. Taylor transferred to Madras.

Major A. V. O'Brien, Staff Surgeon, Murree, assumed charge of the office of Civil Surgeon, Murree, on the forenoon of the 12th April, 1943, in addition to his own duties.

INDIAN LAND FORCES (Emergency Commissions)

To be Major

Daswandi Mall Sachdeva. Dated 5th February, 1943.

To be Captains

Mumtazuddin Ahmad Baqai. Dated 8th January, 1943.

Purnendu Narayan Khan. Dated 28th January, 1943.

5th February, 1943

Syed Mahmud Hassan. Prabhash Chandra Mukerji.

Vidya Sagar. Brahm Govind Prasad.

Pran Nath Chhuttani. Dated 9th February, 1943.

Satya Ranjan Ray. Dated 10th February, 1943.

Nasir Uddin Ahmad. Dated 19th February, 1943.

5th February, 1943

Chokkanna Doreswamy Iyengar.

Hemanta Kumar Ray.

David Satya Nand. Dated 19th February, 1943.

4th March, 1943

Anantharama Rajagopalan.

Abdul Razaq Faruqi.

Arumpool Mathew Francis.

Joseph J. Poovattil.

5th March, 1943

Tarini Prasad Sinha.

Dhirendra Nath Acharyya.

Sanat Kumar Das.

Prosanta Kamal Dutt.

Jagat Jit Singh Bhalla.

Satya Ranjan Chatterji. Dated 6th March, 1943.

Sudhir Chandra Sen Gupta. Dated 6th March, 1939.

Haneef Ahmad Ansari. Dated 7th March, 1943.

8th March, 1943

Suryya Kanta Roy. Man Mohan Nath.

Poondy Gopalatnam.

Sukumara Mitra. Dated 9th March, 1943.

FOR SERVICE WITH THE ROYAL INDIAN NAVY

Shaikh Yonnu Hussain Farooqui. Dated 12th March, 1943.

(Within Indian Limits)

Souri Ranjan. Dated 8th January, 1943.

Syed Balagat Hosain. Dated 6th February, 1943.

(WOMEN'S BRANCH)

To be Captain

(Miss) Sivaramakrishna Padmavati. Dated 8th February, 1943.

(Miss) Kamala Khanna. Dated 14th February, 1943.

The undermentioned officers are transferred to the General Service Cadre, with effect from the date specified.

Captains

S. B. Hosain. Dated 19th February, 1943.

M. D. Azavedo. Dated 20th February, 1943.

R. S. Iyer. Dated 20th February, 1943.

R. Chandra. Dated 14th January, 1943.

Lieutenants

B. V. Rao. Dated 12th February, 1943.

S. Parthasarathy. Dated 19th February, 1943.

To be Lieutenants

Sudhansu Sobhan Maitra and Angarai Narayana-swamy Jagadisan. Dated 5th May, 1942.

Natesh Chandra Sekhar. Dated 27th July, 1942.

Leslie Peter Desouza and William Alexander Lopez. Dated 23rd September, 1942.

Frank Richard Stanford Kellett. Dated 9th October, 1942.

Yash Deva Wahie. Dated 4th December, 1942.

Pallath Govindan Kutty Menon. Dated 14th December, 1942.

George William Gregory Bird. Dated 19th December, 1942.

Frederick Joseph Satur. Dated 28th December, 1942.

Wilfred Edwin Rodgers. Dated 6th December, 1942.

Neel Dennis Walter Morrison. Dated 16th January, 1943.

28th January, 1943

Mohit Kumar Sarkar. Diptiman Bose.

Sachindra Nath Sen. Tara Pada Bhadra.

Amarendra Lal Mukharji.

Carlyle Wilfred Russell D'Rozario. Dated 5th February, 1943.

Kenneth Esmond Tanner. Dated 6th February, 1943.

Lionel Charles Emmett. Dated 10th February, 1943.

12th February, 1943

Bertram John Pereira. Denzil Stanhope Bamford

Eric Patrick O'Neill. Stephens.

13th February, 1943

Ajit Kumar Dawn. Priyotosh Ray.

Satya Bhusan Dutta.

Srimadhava Vasudeo Tungar. Dated 14th February, 1943.

Krishnarao Shantaram Dabholkar. Dated 19th February, 1943.

Alphonso Marshall Lopes. Dated 22nd February, 1943.

Albert William Moody Garrad. Dated 26th February, 1943.

1st March, 1943

Albert James Cadogan. St. John Leger Eling.

5th March, 1943

Edward Anselm Tarleton. Dudley Dayre Stidston.

Sidney Oscar Waller. Dated 6th March, 1943.

Santosh Kumar Das, with effect from 28th November, 1942, and seconded for service in the Indian Air Force, with effect from 8th December, 1942.

18th February, 1943

Mumtaz Husan.

Zahur Ahmed Siddiqui.

Bashir Uddin.

Dinanath Paul Maharaj

Mohammed Akram Chau-

Datta.

dhri.

Makhan Singh Mainii.

Syed Mahmud Hussain Mir Rifat Mahmood.

Jafri.

Mrinal Kanti Mookerjee. Dated 22nd February, 1943.

Mampilly Antony Urumese. Dated 4th March, 1943.

5th March, 1943

Syed Mohammad Moonis Harihar Chandra Ghosh.

Razvi.

Nirmalendu Prakash Sen.

Wilayat Ali Malik.

Charles Richard Peck.

6th March, 1943

Joseph Isidore Rebello.

Narayanaswami Ayyar Chandrasekharan.

Ankala Satyanarayana.

Heywood Ballantyne Gibson.

Dudley John Ridsdale Snow. Dated 7th March, 1943.

9th March, 1943

Vedala Krishnamachary. Pejavar Sadananda Rao.

Frederick Montague Graham. Dated 4th November, 1942.

2nd March, 1943

Hugh Richard Edmund Gillespie.

Sydney Frederick Gomez.

Basil Hector Marten, for service in the Royal Indian Navy. Dated 26th February, 1943.

1st March, 1943

Philip William Weston. Stanley Clarence Gomez.

2nd March, 1943

Allan Peter Maruff. Cecil Herbert Cousins.

Philip Rene Pires. Dated 5th March, 1943.

(DENTAL BRANCH)

To be Lieutenants

Henry Joseph Coombes. Dated 11th February, 1943.

12th February, 1943

Balwant Singh Kochar. Prithvi Raj Gulati.

14th February, 1943

Antonio Dourado.

Coover Phiroze Bharucha.

Madireddi Sabhapathi Rao. Dated 12th February, 1943.

CONTROL of QUININE

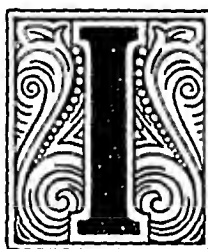
As a war-time measure Quinine
is now under Government
control.



The quality of Howards' Pure
Quinine, Tablets, Ampoules,
etc., is maintained fully up to
the high standard of purity to
which the medical profession
has been accustomed for well
over 100 years.

HOWARDS & SONS LTD. (Est. 1797), ILFORD, LONDON.

Doctors Remember This Pledge



I SWEAR BY APOLLO, the physician, and Aesculapius, and Hygieia, and Panacea and all the gods and all the goddesses — and make them my judges — that this mine oath and this my written engagement I will fulfil as far as power and discernment shall be mine. I will carry out regimen for the benefit of the sick, and I will keep them from harm and wrong .. And now, if I shall fulfil this oath and break it not, may the fruits of art and life be mine, may I be honoured of all men for all time ; the opposite if I transgress and be foresworn.



Excerpts from the Hippocratic oath,
to which physicians have bound them-
selves since the days of antique Greece
LEFT: AESCULAPIUS RIGHT: HIPPOCRATES



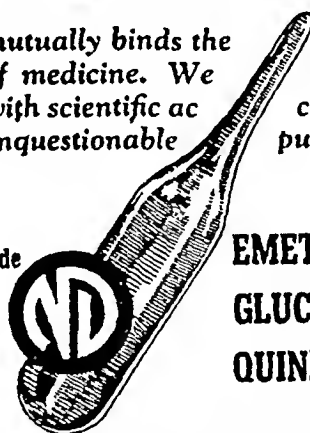
Today, this pledge mutually binds the
the manufacturer of medicine. We
faith by preparing with scientific ac-
ing Injectibles of unquestionable

physician and
on our part, keep
curacy the follow-
purity and efficacy :

ADRENALINE Chloride

CALCIUM Gluconate

DIGITALIN



EMETINE Hydrochloride

GLUCOSE Solution

QUININE-Bi-Hydrochloride

NATIONAL DRUG CO. LTD.

Biological Laboratories

Managing Agents · H. Datta & Sons Ltd. 15, Clive Street, Calcutta

5th March, 1943

Yeshwant Shankar Pra- Manoranjan Dass Gupta.
 dhan. Chowdhury Mozaffor Ali
 Dundappa Shivalingappa Beg.
 Patil. Anthony Arthur D'Souza.
 Chimanbhai Chhotabhai Abu Yusuf Mahammad
 Patel. Nuruddin.
 Yogindra Sain Sawhney.

LEAVE

Lieutenant-Colonel H. E. Murray, Professor of Mid-
 wifery, Medical College, Calcutta, and Superintendent,
 Medical College Hospitals, Calcutta, is granted leave
 for 1 month, with effect from the 16th May, 1943.

PROMOTIONS

Lieutenant-Colonels to be Colonels

R. Lee. Dated 28th November, 1942.
 R. Hay, C.I.E. Dated 21st February, 1943.

Majors to be Lieutenant-Colonels

D. Kelly. Dated 1st February, 1943.
 K. R. Sahgal. Dated 26th March, 1943.
 K. M. Bharucha. Dated 13th April, 1943.

*(Emergency Commissions)**Captains to be Majors*

M. S. Rao. Dated 22nd October, 1942.
 P. I. Franks. Dated 23rd April, 1943.

The undermentioned officers are confirmed in their
 rank with effect from the date specified :—

Captains

S. Pal. Dated 8th December, 1941.

4th February, 1942

A. T. George. I. Chand.

O. P. Markandya.

L. M. Ram. Dated 21st February, 1942.

M. S. Babbar. Dated 5th March, 1942.

15th March, 1942

A. S. Sen. K. G. Kapoor.

M. U. Hayat. Dated 13th March, 1942.

A. F. Lasrado. Dated 15th April, 1942.

V. G. Dabholkar. Dated 18th April, 1942.

S. C. Chatterji. Dated 4th May, 1942.

5th May, 1942

B. D. Gupta. N. K. Acharyya.

T. K. Chary. M. R. Beg.

A. K. Mitra. S. D. Surie.

N. C. Mehta. L. S. Zuzarte.

N. K. Sen. S. B. S. B. Bhalla.

B. Lal. B. K. Chowdhuri.

G. K. Mitra. N. C. Banerjee.

R. S. Saha. S. V. Tilak.

H. K. Mitra. K. Banerjee.

M. N. Razdan. P. K. Mukerjee.

D. C. Bhar. R. D. Irani.

A. W. Lisboa. G. P. Sathe.

S. S. Grewal. K. H. Bhadhbade.

Abdul Rashid. B. V. Shirolkar.

H. C. Dhawan. P. N. Bagchi.

S. Gopalaswami. S. V. Velankar.

6th May, 1942

K. L. George. N. C. Ghosh.

B. N. Chatterjee. A. G. Chaudhuri.

P. V. Kurian. S. K. Bose.

H. DeSouza. S. S. Nazir.

B. G. Sur. H. R. Ohrie.

D. R. Bharucha. Dated 18th May, 1942.

M. A. Sami. Dated 4th June, 1942.

5th June, 1942

H. S. A. Malik. A. C. Bose.

P. C. Basu. S. A. Ali.

A. K. Ray. H. P. Rao.

H. C. Banik. J. Singh.

S. N. Seal. N. K. Basu.

B. De. N. G. Mukerjee.

M. K. Ray. S. N. Ahmed.

B. S. Khangura. B. K. Banerjee.

J. K. Gharpure. D. L. Bhagwat.

D. L. De. M. Banerjee.

S. B. Mitra. P. B. Koppiker.

A. Mascarenhas.

6th June, 1942

A. M. Khan. B. E. Pardiwalla.
 M. G. Prabhu. Dated 8th June, 1942.
 G. Venkataramaniah. Dated 9th June, 1942.
 N. Narayanan. Dated 10th June, 1942.
 D. S. Pathre. Dated 15th June, 1942.
 M. Z. Ullah. Dated 22nd June, 1942.
 R. Bhattacharya. Dated 29th June, 1942.

3rd July, 1942

M. A. G. Bhutty. J. C. Sharma.
 S. Chakrabarti. J. N. Karande.
 K. C. Saha. S. Govindarajan.
 A. K. Bose. A. Sayeed.
 B. S. Dutt. S. K. Dutta.
 R. M. Dastur. L. K. Chakraburty.
 R. B. More. S. N. Sinha.
 M. L. Datta. B. Guha.

4th July, 1942

N. K. Basu. S. M. K. Wasti.
 K. Somayya. Dated 5th July, 1942.

9th July, 1942

T. K. Raju. C. R. Krishnaswami.
 N. G. D. Sarkar. Dated 10th July, 1942.
 J. Nichani. Dated 13th July, 1942.
 H. A. Bali. Dated 16th July, 1942.

7th August, 1942

K. S. Rau. B. Prasad.
 M. Sen. D. P. Chakrabartty.
 D. C. Basak. B. N. Maji.
 M. S. Rao. P. Banerje.
 B. K. Sen. C. Suryanarayana.
 S. C. Nath. J. M. Lewis.
 P. P. Ghosh. J. M. Pinto.
 G. K. Roy. S. C. Paul.
 P. C. Mallik. A. T. DeSouza.
 A. Sen Gupta. J. R. Pereira.
 A. N. Basu. S. K. Sen.
 H. Dubey. D. Sen.
 S. Mukherjee. N. N. Ghosh.

8th August, 1942

B. R. Mahajan. B. B. Vaidya.
 J. Ayaram. N. G. Rajulu.

12th August, 1942

A. B. Rustom. M. Amin.
 Z. M. Pandher. Dated 15th August, 1942

4th September, 1942

K. N. Sen. B. V. Rao.
 R. L. Krishnaswami. A. M. Mobsby.
 C. S. Sandhu. I. Singh.
 S. A. Rahim. S. K. Sen.
 M. M. Singh. S. R. Kidiyoor.
 B. Lall.

5th September, 1942

L. M. Gupta. O. K. T. Kesavan.
 S. N. Ray.
 G. S. Balasubramaniam. Dated 6th September, 1942.

7th September, 1942

G. S. Majumder. B. S. Row.
 S. P. Subramaniam. V. C. Kamaraju.

8th September, 1942

S. M. Ghosh. B. Ramachandran.
 R. Natarajan. Dated 9th September, 1942.
 E. Dikshitulu. Dated 21st September, 1942.
 E. K. P. Nambiar. Dated 24th September, 1942.
 E. C. Srinivasan. Dated 28th September, 1942.

Lieutenants

5th May, 1942

R. Kumar. Abdur Rashid.
 A. D. Papneja.

5th June, 1942

A. Karim. H. S. Jawanda.
S. Lite. M. Iqbal.
S. I. R. Sarma. K. C. Ganapathy.
K. Umapathi. W. M. S. Jonas.
R. Rajagopalan. N. R. Ramkrishnan.
J. Srinivasan. E. J. D'Netto.
S. R. N. A. Babu. V. P. Rangaswami.
S. B. H. Gardezi. V. Selvaraj.
T. M. Seethapathy. S. K. Banerjee.
R. N. Chopra. S. Krishnan.

R. R. Rao.

6th June, 1942

A. P. Babu. M. Rahimulla.

7th June, 1942

A. Shetty. E. P. Gonsalves.

8th June, 1942

S. P. Vedachalam. D. A. Narasimhan.

3rd July, 1942

P. P. Balkrishnan. P. V. Rao.
Z. H. Syed. A. Husain.
K. S. Radhawa. R. A. Mehta.
R. Singh. G. S. Godiwalla.

7th August, 1942

C. T. Ramachandran. S. S. Bisht.
K. D. Ganguly. M. Satyanarayana.
P. F. Verghese. S. Das.

P. N. K. Menon.

S. Parthasarathy. Dated 8th August, 1942.

G. G. Prabhu. Dated 11th August, 1942.

P. S. Sehra. Dated 14th August, 1942.

A. Hamid. Dated 15th August, 1942.

4th September, 1942

S. A. Narayanan. S. H. Massey.

V. A. Damodaram.

5th September, 1942

G. Mandal. M. Anantasayanam.

H. S. Saksena. A. C. K. K. Raja.

M. Swaminathan. Dated 6th September, 1942.

K. G. Raj. Dated 7th September, 1942.

D. Ramanath. Dated 8th September, 1942.

A. K. M. M. Rahman. Dated 14th September, 1942.

The undermentioned officers are confirmed in their rank, with effect from the date specified :—

Captains

(Miss) P. S. Davar. Dated 8th April, 1942.
(Miss) D. M. J. Stracy. Dated 17th April, 1942.
(Mrs.) S. L. Bhatia. Dated 2nd May, 1942.
(Miss) F. P. Wadia. Dated 4th May, 1942.
(Miss) R. H. Fonseca. Dated 19th May, 1942.
(Miss) M. W. Beeby. Dated 31st May, 1942.
(Mrs.) M. R. Tarapore. Dated 1st June, 1942.
(Mrs.) C. I. M. Drummond. Dated 1st June, 1942.
(Mrs.) R. K. Puri. Dated 1st August, 1942.
(Mrs.) E. M. McDonald. Dated 5th August, 1942.
(Miss) M. T. D'Silva. Dated 5th August, 1942.
(Mrs.) E. H. Barrington. Dated 7th August, 1942.
(Miss) A. L. F. Hankins. Dated 8th August, 1942.
(Miss) U. Roy. Dated 8th August, 1942.
(Miss) J. B. V. Raj. Dated 14th August, 1942.
(Miss) A. M. Waters. Dated 18th August, 1942.
(Miss) S. M. Rapson. Dated 19th August, 1942.
(Miss) P. B. Bellhart. Dated 21st August, 1942.
(Miss) B. M. Burgess. Dated 24th August, 1942.
(Miss) E. Mitra. Dated 29th August, 1942.

Lieutenants

(Miss) L. Bhargava. Dated 11th April, 1942.
(Miss) H. K. Nanjamma. Dated 11th August, 1942.
(Miss) A. Mathew. Dated 17th August, 1942.

Lieutenants to be Captains

C. Venkaiah. Dated 28th May, 1941.
21st November, 1941

M. A. Khan. H. K. Musazai.

R. S. Gupta.

S. N. Chatterjee. Dated 11th December, 1942.

R. K. Das. Dated 28th December, 1942.

J. G. H. Davidson. Dated 6th November, 1942.

W. B. Johnston. Dated 4th December, 1942.

H. R. Anand. Dated 25th February, 1942.

E. E. Vaughan. Dated 5th August, 1942.

5th May, 1942

S. S. Maitra. A. N. Jagadisan.
Y. D. Wahie. Dated 4th December, 1942.
N. C. Sekhar. Dated 27th July, 1942.
P. G. K. Menon. Dated 14th December, 1942.
A. Chatterjee. Dated 19th November, 1942.
H. A. Press. Dated 25th February, 1943.
A. S. Manuel. Dated 2nd March, 1943.
V. Sankariah. Dated 3rd March, 1943.

(WITHIN INDIAN LIMITS)

Lieutenant to be Captain

G. I. Ramachandran. Dated 8th December, 1942.

Lieutenants (on probation) to be Captains (on probation)

V. Venkatasubramanian. Dated 10th January, 1942.

D. M. Goghavala. Dated 5th March, 1942.

Miss G. M. Higgins. Dated 25th November, 1942.

S. K. Bose. Dated 25th February, 1943.

M. K. Ray, A. C. Bose, and S. K. Banerjee. Dated 10th March, 1943.

RETIREMENTS

Colonel H. Horan-Brown. Dated 28th March, 1943.

Lieutenant-Colonel J. R. Katariya. Dated 18th February, 1943.

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Original Articles

CASES OF INTEREST SEEN AT THE RADIOLOGICAL DEPARTMENT OF THE ERSKINE HOSPITAL, MADURA, DURING 1941 AND 1942

By SRI S. SUBRAMANYAM

(Civil Assistant Surgeon)
Radiologist, Erskine Hospital, Madura

MADURA, a town of roughly a quarter million inhabitants, is the largest city in India south of Madras. The Erskine Hospital was opened in 1940, and has accommodation for 537 patients. It is one of the most up-to-date mofussil hospitals in India. Here are given a few brief notes together with the skiagrams of some of the cases of interest that passed through the radiological department in 1941 and 1942.

Nervous system (plate XV)

Figure 1.—Pituitary tumour. The skiagram shows the sella turcica greatly enlarged.

Figure 2.—Spinal tumour. Cisternal puncture with injection of neo-hydrinol; shows the neo-hydrinol held up by the tumour at the level of the 4th dorsal vertebra.

Respiratory system (plate XV)

Figures 3 and 3a.—Cystic bronchiectasis in a girl of 14, with very few physical signs, but with the condition clearly shown by neo-hydrinol injection.

Figure 4.—Tumour of left lower lobe of lung in a woman of 35. A filling defect is seen after neo-hydrinol injection, in the lower middle zone.

Circulatory system (plate XV)

Figure 5.—Congenital heart disease. A girl of 14 with cyanosis of lips and finger nails, with a loud systolic murmur in the pulmonary area, conducted up to the outer side of sterno-clavicular junction on both sides. The heart shows hypertrophy of the left ventricle—boot shape in outline—and widening of the upper mediastinal shadow. Co-arcuation of aorta?

Figure 6.—A boy of 15 admitted for dyspnoea. A systolic thrill in the pulmonary area, and a loud systolic murmur conducted from the pulmonary area to the left side of neck. X-ray shows an enlarged heart with extra prominence of the conus arteriosus.

Digestive system (plates XV and XVI)

Figures 7 and 7a.—A case of regional jejunitis. In the 1st skiagram, taken 5 minutes after the barium meal, there is a more-or-less homogeneous filling of the jejunum instead of the usual feathery appearance; and in the 2nd picture, taken at 3 hours, spots of barium are seen sticking to some places after these coils have generally emptied. Operation confirmed

the diagnosis and the pathologist's report on the resected portion of jejunum was 'Non-specific granulomatous ulceration; no evidence of tuberculous infection'.

Figure 8.—A case of multiple peptic ulcers. The skiagram shows an accessory pocket of a large perforating ulcer in the lesser curvature, and another ulcer in the pre-pyloric region, causing stenosis and six-hour retention of the barium meal in the stomach; diagnosis confirmed at operation.

Figure 9.—A case of carcinoma of the head of clinically, bilateral lumps were felt in the duodenal 'C' curve, and pressure deformity of the stomach; confirmed at operation.

Urinary system (plate XVI)

Figure 10.—A case of polycystic kidneys: clinically, bilateral lumps were felt in the hypochondrium. X-ray examination (after injection of pyelectan) shows gross enlargement of the kidneys and the pelvis, and irregular enlargement of the calices.

Figure 11.—A case of bilateral hydronephrosis (with a co-existing branched renal calculus in the left side) in a lad of 18 years. The tumour was of considerable size on the right side, and the right kidney function was defective, and the dye concentration poor. The renal pelvis and calices are not visualized on the right side in the skiagram, which was taken 20 minutes after the injection.

Skeletal system (plates XVI and XVII)

I. *Injuries*: *figure 12.*—A case of fracture-dislocation of the 2nd lumbar vertebra, with no sensory loss and no loss of visceral reflex, but with paresis of the lower extremities, more marked on the left side. For such gross displacement, the injury to the cord or cauda equina was negligible.

Figure 13.—Fracture-dislocation of the head of the radius due to a fall from a tree. The broken head lies in the medial aspect of the elbow.

II. *Diseases*: *figures 14 and 14a.*—A case of Paget's disease in a girl of 20 years. She was referred to the Radiological Department for ? T.B. hip. Besides changes elsewhere, the pelvis shows a 'woolly' appearance, and localized diffuse increase in density, with obliteration of the cancellous trabeculae in these dense areas. In the skull, linear areas of condensation and osteoporosis are seen side by side, and there is marked enlargement of the sphenoidal sinus. (Osteitis deformans is rather uncommon under forty.)

Figure 15.—A case of syphilis of the skull, in a man of 50 years, with a history of syphilis 15 years ago. Frequent attacks of headache forced him to seek hospital aid.

The skiagram shows irregularity of the outline, affecting both the tables, and areas of bone destruction and sclerosis side by side.

(Concluded on next page)

A NOTE ON VITAMIN B₁ AND EXPERIMENTAL PEPTIC ULCER

By M. N. RAO

BRADFIELD (1928), McCarrison (1921) and Somervell and Orr (1936), the pioneer workers on the problem of the aetiology of peptic ulcer in India, were unanimous in their opinion that the 'poor Madras diet' has a direct relationship to the common incidence of the disease in South India. In this connection, figures other

(Continued from previous page)

Figure 16 (plate XVII).—A case of mycetoma. This is one of several cases especially studied for determining the radiological appearances. In a well-developed case, a fibrocystic degeneration is the usual finding, though in the early stages, hardly any bony changes are noticeable. The radiograph shows absorption of cancellous trabeculae, and the formation of cyst-like areas, chiefly over the bases of the metatarsals and the adjoining tarsus. The periosteal changes in the 5th metatarsal are conspicuous.

Figures 17 and 17a.—A case of ? Albers Schonberg's disease (marble bones), in an adult of 60 years, referred to the x-ray department for ? fracture of neck of femur. Several of his bones showed unmistakable marbling, and optic atrophy was present; but there was no 'club like' appearance of the tibial extremities of the femur, nor was there any characteristic tufting of the skull that goes with osteitis deformans.

Figure 18.—A case of rickets in a child of 11 years admitted for bilateral genu valgum.

X-ray examination reveals, besides changes in other bones, marked changes in the elbow joints, which are unusual. In the wrist, the radius shows the typical wine glass deformity (cupping) of the diaphyseal end, and the ulna is longer than the radius.

Miscellaneous (plate XVII)

Figures 19 and 19a.—A strange type of fistula. The radiograph shows the track connecting the abdominal wall with the trachea, through the right bronchus (when BIP was injected into the sinus in the right abdominal wall, it was coughed up into the mouth). The fistula was the result of a tumour of two years' duration in the right hypochondrium, which burst of itself.

Figure 20.—A case of endocrine disturbance in a married woman of 21 who was admitted for sterility and amenorrhoea. She was fat and had the facies of a child. The uterus was of the infantile type. X-ray of the skull shows hyperostosis of the frontal and parietal bones, and a rather small sella.

My sincere thanks are due to Lieut.-Colonel A. S. Leslie, I.M.S., Superintendent of this hospital, for his valuable suggestions and permission to make use of the hospital records.

than those already published (Rao, 1939) from different areas where people consume 'poor Madras diet' are interesting additional reading. Figures from the Osmania Hospital, Hyderabad, for the years 1931-35 show that 0.63 per cent of operations were for peptic ulcer. Similarly in Ceylon (Fernando, 1940) the number of operations for peptic ulcer ranged from 0.5 per cent (1939 General Hospital statistics) to 2.0 per cent (Dr. Gabriel's). Of all the various constituents of diet that have an influence on the gastrointestinal tract, vitamin B₁ is one of the important ones, and recent literature has many references to the influence of vitamin B₁ on the pathology of stomach. Moreover, vitamin B₁ happens to be also one of the deficient food principles in the poor Madras diet (Rao, 1939).

With the idea of studying the effects of vitamin B₁ deficiency on the stomach, a preliminary experiment was conducted and is reported below. For brevity the complete discussion is omitted, and only relevant points are emphasized.

Experiment

Twelve pups from two litters formed the experimental group. Before the experimental diet was commenced, the animals were weaned and later were given small quantities of cow's milk. All the pups were given a dose of anthelmintic prior to the experiment. The experimental diet was as follows:—

Milk and raw milled rice were autoclaved for one and a half hours. The rice was boiled with a little crude common salt and served with warm milk. Three drops of 'Adexolin Glaxo' were added in the morning feed for each animal, and half a tablet (25 mg.) of vitamin C (Redoxon-Roche) every second day. This diet yields nearly all the dietary essentials except the B group of vitamins.

The animals were kept in hygienic surroundings in well-ventilated enclosures.

The twelve dogs on which this report is based were autopsied either during or at the end of the experiment. The observations are given as a series of short protocols.

Dog 1. Diet taken for 21 days—died. On post-mortem examination, a minute erosion of the mucous membrane of the first part of the duodenum and a mild round worm infection were found.

Dog 2. Diet taken for 69 days—died. No abnormality on post-mortem examination.

Dog 3. Diet for 76 days; killed in good health by intracardiac ether. All the abdominal organs were normal.

Dog 4. Diet for 77 days—died on the 78th day. In the last two weeks the animal did not take the feeds properly. Post-mortem examination revealed nothing abnormal.

Dog 5. Diet for 92 days; during the course of the experiment it developed ataxic gait and aversion to food, and died. Examination of the viscera showed nothing abnormal. The stomach was dilated.

Dog 6. Diet for 93 days. During the last two weeks, the animal showed aversion to food and was not active. The post-mortem examination showed the small intestine slightly ballooned out in two or three areas and a shallow duodenal ulcer in the first part of

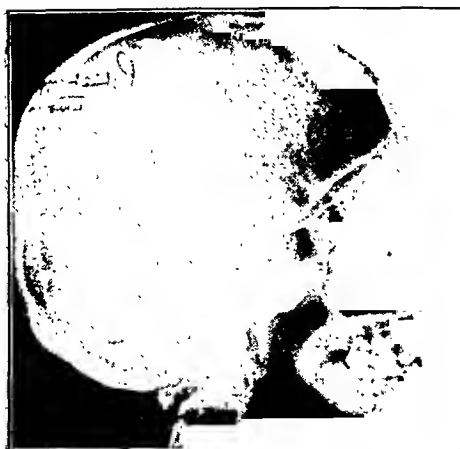


Fig. 1.—Pituitary tumour.



Fig. 2.—Spinal tumour.



Fig. 3.—Cystic bronchiectasis.
(A.P. view.)



Fig. 3a.—Cystic bronchiectasis.
(Lat. view.)



Fig. 4.—Tumour of lung.

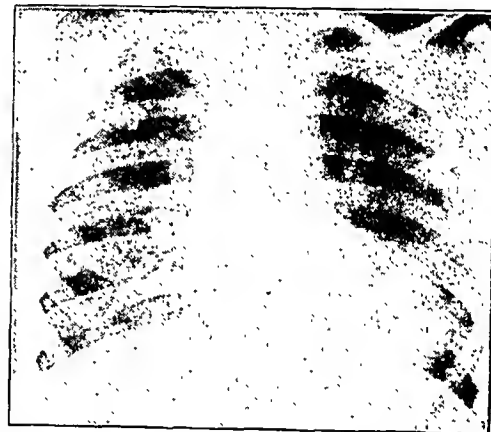


Fig. 5.—Congenital heart with boot-shaped left ventricle.

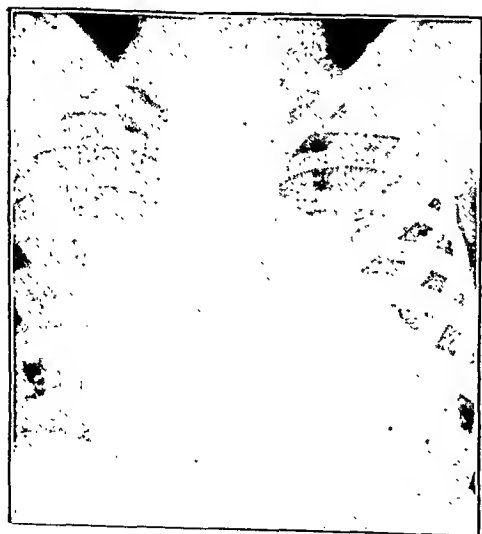


Fig. 6.—Congenital heart disease. ? Patent ductus arteriosus.



Fig. 7.—Regional jejunitis (5 minutes after barium meal).



Fig. 7a.—Regional jejunitis (3 hours after barium meal).

PLATE XVI

CASES OF INTEREST SEEN AT THE RADIOLOGICAL DEPARTMENT, ETC. : S. SUBRAMANYAM



Fig. 8.—Accessory pocket of a perforating gastric ulcer and a pre-pyloric ulcer.

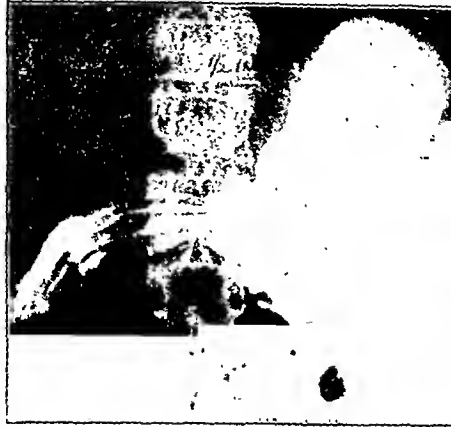


Fig. 9.—A case of carcinoma of head of pancreas causing marked widening of duodenal 'C' curve.



Fig. 10.—Polycystic kidneys.



Fig. 11.—Hydronephrosis and renal calculus.



Fig. 12.—Fracture-dislocation of spine.



Fig. 13.—Fractured head of radius.



Fig. 14.—Pelvis in Paget's disease.



Fig. 14a.—Paget's disease; skull showing a large sphenoidal sinus.

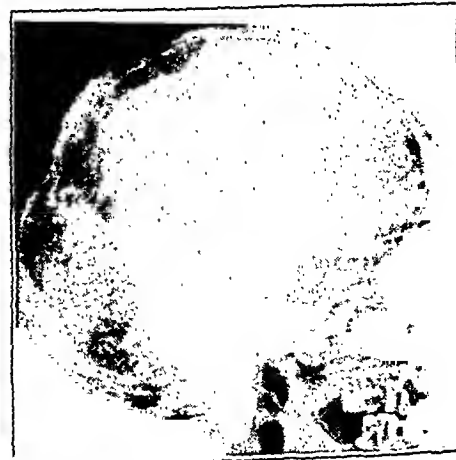


Fig. 15.—Syphilis of skull.



Fig. 16.—Mycetoma.



Fig. 17.—? Marble bones (Albers Schonberg's disease).

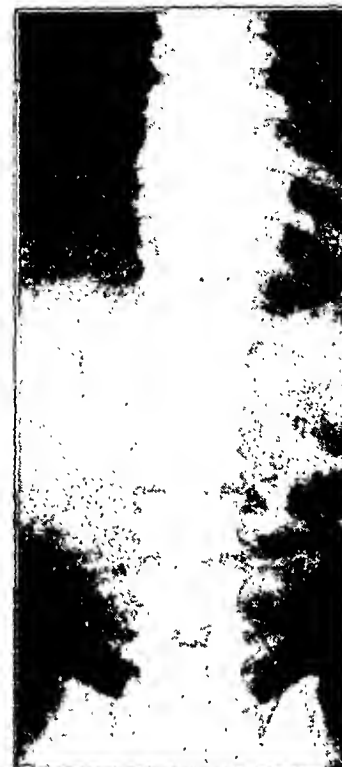


Fig. 17a.—? Marble bones (Albers Schonberg's disease)



Fig. 18.—Rickets.



Fig. 19.—A strange type of fistula. (A.P. view.)



Fig. 19a.—A strange type of fistula. (Lat. view.)

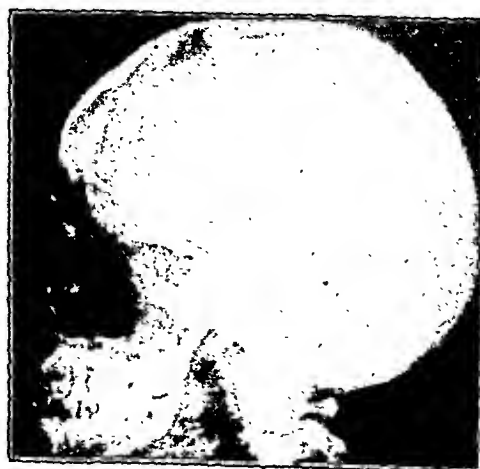


Fig. 20.—Skull in a case of endocrine disorder.



Fig. 1.—The duodenum and the lesser curvature of the stomach of dog 6: showing an erosion in the former and a chronic ulcer in the latter.



Fig. 2.—The pyloric antrum and the first part of the duodenum of dog 12: three acute erosions in the duodenal wall are seen.



Fig. 3.—A chronic peptic ulcer in the pyloric antrum of dog 7.

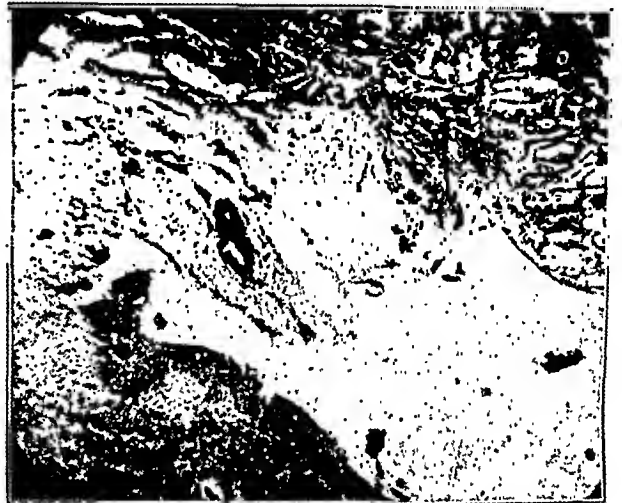


Fig. 4.—A photomicrograph of the ulcer in figure 3, showing the fibrosed base of the ulcer and the overhanging gastric mucosa at the margin.

PSAMMOMA OF THE CHOROID PLEXUS IN A CASE OF PULMONARY TUBERCULOSIS :
J. F. COLTMAN AND B. P. TRIBEDI (PAGE 326)

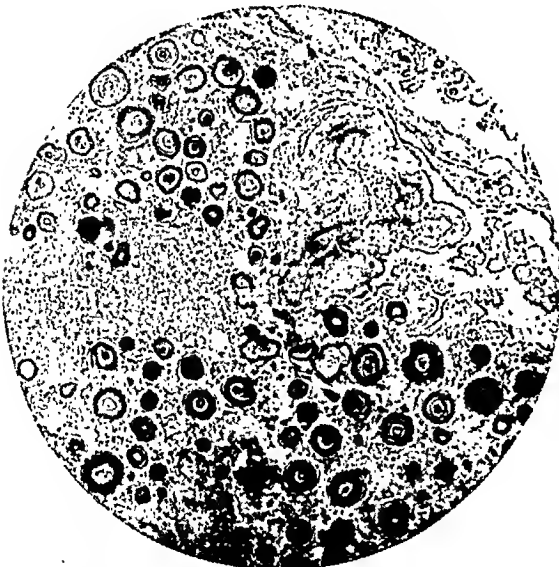


Fig. 1.—Low power photomicrographic view of the section from the tumour showing hyalinization and calcification of vessels and perivascular spaces.



Fig. 2.—High power photomicrograph of the previous one showing complete calcified area.

the duodenum and a chronic gastric ulcer in the lesser curvature of the stomach (plate XVIII, figure 1).

Dog 7. Diet for 95 days. Killed by intracardiac ether. Post-mortem examination showed a dilated stomach, a chronic gastric ulcer in the lesser curvature near the pylorus, and a cicatrix of the mucous membrane in the body of the stomach (plate XVIII, figure 3).

Dog 8. Diet for 97 days—died. Post-mortem examination showed a cicatrix in the pylorus, suggesting a healed pyloric ulcer.

Dog 9. Diet for 104 days. After about six weeks the animals developed ataxic gait and developed aversion to food and gradually died of starvation. Post-mortem examination showed free fluid in the peritoneal cavity and nothing abnormal in the gastro-intestinal tract.

Dog 10. Diet for 111 days. In good health throughout and was killed by intracardiac ether. Post-mortem examination showed nothing abnormal.

Dog 11. Diet for 119 days. After about two months, the animal became very sickly with severe cutaneous infection. The animal kept indifferent health and was killed by intracardiac ether. Post-mortem examination showed advanced fatty degeneration of all the abdominal organs. The mucous membrane of the gastro-intestinal tract was pale and no ulcers or erosions were seen. The stomach was dilated.

Dog 12. Diet given for 119 days. The animal was very healthy during the experimental period except for the last three weeks when it did not take its feeds properly. On autopsy three peptic ulcers were found in the first part of the duodenum (plate XVIII, figure 2).

In general, the majority of the animals showed a poor appetite towards the end of the experiment.

A low magnification photomicrograph of the section of ulcer in figure 3 is given in plate XVIII, figure 4.

Discussion

The results of investigation on the pathology of the stomach in experimental vitamin B₁ deficiency are conflicting.

One school of thought believes that the stomach is affected through the nervous system which in turn is affected in B₁ deficiency. It appears also that not only the central nervous system but even the efferent nerves of the stomach may be involved. However, in vitamin B₁ deficiency, apart from the nervous influences, changes in both the gastric motility and gastric secretion have been reported.

Lowered gastric motility in B₁ deficient animals has been described by Cowgill *et al.* (1926), Stucky, Rose and Cowgill (1928), Rose and Stucky (1930) and Gal (1930). Gastric distension in B₁ deficiency animals has been described by Rowlands and Browning (1928) and Moore, Plymate and Andrew (1932). In three of the dogs reported in this series also, there was evidence on post-mortem examination of gastric distension.

The consensus of opinion with regard to the gastric secretion is that B₁ deficiency leads to hypochlorhydria, but some authors (McCarrison 1931; Dalldorf and Kellogg, 1932) have reported erosions and ulcers of the stomach, which are usually associated with hyperchlorhydria. In

the present series also, three of the animals show definite evidence of chronic peptic ulcer either in the stomach or duodenum. How far these ulcers are attributable to vitamin B₁ deficiency is a point for consideration. In B₁ deficiency, one of the very early and characteristic symptoms is anorexia. Though it is a constant symptom leading ultimately to partial or complete starvation of the animal, the pathogenesis of this anorexia is not clear. It appears to be more a functional change than an organic change. However, it may be argued that the pathological changes in advanced vitamin B₁ deficiency may be brought about to a certain extent by the concurrent inanition. It is therefore rather difficult to attribute organic changes to vitamin B₁ deficiency alone. Chatterjee (1935) and Vedder (Williams and Spies, 1938) have come to this conclusion.

Summary

A preliminary experiment of the effect of vitamin B₁ deficiency diet on the stomach of dogs is described.

Five in a series of twelve, developed peptic ulcer, three being chronic.

It is not certain to what extent the stomach lesions are the direct result of vitamin B₁ deficiency.

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PSAMMOMA OF THE CHOROID PLEXUS IN A CASE OF PULMONARY TUBERCULOSIS

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MENINGEAL endotheliomata are by no means uncommon. They usually appear as (a) a perivascular endothelioma or (b) as psammoma where the perivascular units undergo hyalinosis and calcification (Ewing 1931). This latter group is not a very common finding, at least in India. On going through the records of the last 40 years of the Pathology Department of Calcutta Medical College we have not come across a single case of this type of neoplasm. Moreover tumours of the choroid plexus of ependymal origin are comparatively rare (Ewing, *loc. cit.*). In consideration of these facts it seems justifiable to record the following case of psammoma of the choroid plexus which represents features of interest from more than one aspect.

Case.—European widow, aged 38 years, refugee from Burma.

24th August, 1942.—Complained of sickness and diarrhoea, duration two days. No pains in abdomen. Had had headache and slight fever a week previously, with heavy cold.

Had been listless since arriving in Calcutta at the end of June 1942. On most days brought up a little sputum, slightly yellow. History of tuberculosis of right lung with two cavities in 1936-37. Treated at St. George's Hospital, London, where a right phrenic avulsion was done.

Examination showed her to be pale but well nourished. Throat: slight redness of fauces; tonsils had been removed previously, with much scarring. Tongue: slightly grey coated posteriorly. Chest: both sides moved equally on respiration; a few fine crepitations were present at right apex, anteriorly and posteriorly. Heart: apex within nipple line, sounds normal. Pulse 60. Abdomen: slight tenderness and gurgling in epigastrium and in ascending colon.

25th August, 1942.—Stool showed amœbic cysts and a few R.B.Cs and pus cells. Culture negative.

27th August, 1942.—Felt well and was up and about. Taking stovarsol tablets, gr. iv, one, twice daily, after food, for ten days.

5th September, 1942.—Stated that she had had fever for about 24 hours, and that a rash had come out. Her head felt 'muzzy' she thought due to the fever, but there was no severe headache, or aches or pains elsewhere in the body.

Examination.—Temperature 102.8°, pulse 96. Eyes and face puffy, and conjunctivæ reddened. Face, neck and shoulders covered with a bright scarlatiniform rash completely covering the skin and causing it to appear slightly thickened and oedematous. The rash was least marked on the thighs and legs, where small red patches were present. Mouth: no Koplik's spots, tongue slightly grey coated. Glands: post cervical glands were very markedly enlarged, firm and discrete, but not tender. Abdomen: slight tenderness still present but less than on 24th August, 1942.

The facts that the rash came out within 24 hours, and that she had no generalized severe aches and pains, were against it being a dengue fever, although there were many cases in Calcutta at that time. Another

possibility that was thought of was an arsenical dermatitis from the stovarsol tablets. She had already taken 19 out of the 20 tablets prescribed. Against an arsenical poisoning was the cervical adenitis and the fact that the skin was not particularly irritable. To be on the safe side the final tablet was omitted. The only other probability was German measles, although close questioning did not reveal any likely contacts, and no cases had been encountered for about six months before this. She was told that it was probably German measles and that there was nothing to worry about.

7th September, 1942.—She was seen again to-day because 'she did not feel well'. She could not express herself any more definitely than this. She had no pain of any description. Temperature 99°, pulse 76. Rash was still present, fading from upper areas but more marked on legs. Posterior cervical glands still very much enlarged. Nothing else abnormal could be found.

2 p.m.—Her bearer stated that she suddenly had a 'fit', screamed at the top of her voice and became unconscious. Respirations became very slow.

3 p.m.—When seen at 3 p.m. respirations were slow (10 per minute), laboured and rather sighing. Slight cyanosis. Pupils equal. Pulse 64. Left arm slightly spastic, plantar reflexes flexor. Passed a stool in bed clothes. Inj. coramine 2 c.cm. given and sent to the hospital in an ambulance.

4 p.m.—On arrival at hospital, was still unconscious, and pulse was hardly perceptible. Condition very serious. Rash still present all over.

Both arms spastic, knee jerks and ankle jerks slightly increased, plantar reflexes flexor.

5 p.m.—Temperature 100°, pulse 80, respiration 8. Pupils equal, reacted to light, slightly dilated. Began to have typical epileptiform fits and remained in a condition of status epilepticus.

A lumbar puncture was done, and 10 c.cm. of clear fluid was withdrawn; pressure moderately increased.

9 p.m.—Temperature 105° (axilla), pulse 130, respiration 32. Inj. morph. hypo. gr. 1/6th given, and fits stopped for three hours, but started again at midnight. Controlled again by giving paraldehyde per rectum.

Laboratory findings.—

Stomach wash (done on admission), nothing abnormal.

Urine: albumin present and pus cells. Culture *B. coli communis* a few colonies (? contamination).

Stool: growth of *B. pseudocarcinarius*.

Blood for M.P.: negative.

Blood picture: R.B.C's 4,050,000; hæmoglobin 70 per cent; W.B.C's 14,500; neutrophils 72 per cent; eosinophiles 1 per cent; lymphocytes 23 per cent; monocytes 4 per cent.

C.S.F. Micros.: no cells or micro-organisms; culture, sterile. (Fluid for chemical tests apparently went astray.)

Vaginal swab: a few pus cells, no Gram-negative diplococci. Culture *B. coli communis* and *Staph. aureus*. Wassermann reaction: weakly positive.

9th September, 1942.—Patient remained unconscious, and temperature varied between 102° and 105°. Although blood reports were negative, quinine bihydrochloride gr. x was given intragluteally at 10 p.m.

10th September, 1942.—Unconscious still. Temperature 106° at 12 noon. Quinine gr. x repeated intragluteally. 100 c.cm. of 25 per cent glucose given intravenously as she was unable to swallow, and injections of coramine p.r.n. Besides this she got injections of ascorbic acid 100 mgm. daily. Being unconscious for so long, her chest became congested, and her cough increased. Drogenan sodium was given daily.

12th September, 1942.—10 a.m. Temperature 97.6°. The temperature had fallen steadily since 12 noon on the 10th when it reached the maximum of 106° by 6 p.m. Pneumonic patches posteriorly.

13th September, 1942.—Very cyanosed. Pulse small and rapid. Semi-conscious. Gradually got worse.

14th September, 1942.—Died at 2.55 a.m. Post mortem at 1 p.m. Chest: dense pleural adhesions on both sides, especially over apices. Right lung appeared atrophied. Upper lobe in a state of red hepatization

and much fibrous scarring. *Left lung*—many pneumonic patches in upper lobe with recent small cavity at apex.

Abdomen : a few peritoneal adhesions, otherwise normal.

Womb : infantile.

Brain : Meninges congested. Excess of C.S.F. Substance slightly oedematous. Left lateral ventricle pink and congested. A small pinhead nodule, ? a tubercle, slightly yellowish in colour, found in left choroid plexus. A small hæmorrhage in subcortical substance of right parietal region. The brain was cut in thin slices but no other hæmorrhages were found.

Micro-sections of the choroid plexus showed numerous perivascular areas of hyalinization (figure 1, plate XVIII). Some of these areas have undergone calcific changes (figure 2, plate XVIII). Some of the vessels have also undergone similar changes.

Commentary and discussion

These hyalinized and calcified areas seen in the sections account for the tubercle-like nodule seen in the choroid plexus. Divergent opinions have been expressed as to the origin of such a tumour. Kettle (1925) considered the majority of these tumours simply as angiomatous, calcification taking place as a secondary phenomenon either in capillary thrombi or in groups of proliferated endothelial cells or even in the walls of the swollen vessels. Consequently these tumours are classified as endotheliomata. Mallory (1920) denied their endothelial origin. According to him there is no dural endothelium but the inner surface of the dura is bare except for fibroblasts, and he opined that these tumours are fibroblastic in origin. Boyd (1938) suggested that the original name of psammoma given by Virchow should be discarded as these psammomas or 'sand grains' are nothing but a degenerative stage of the endothelial tumours. He described psammoma bodies as hyaline spherical bodies showing concentric lamination and similar to corpora amylacea except that they contain lime salts. Ferraro and Damon (1931) discussed the origin of amyloid bodies in the central nervous system. They summarized the various theories of their origin into the following groups : (a) the neurogenic theory which claimed the axis cylinders and the myelin sheaths as being the origin of the amyloid bodies, (b) the gliogenic theory—the amyloid bodies arising from the glial element, (c) the lymphogenic theories—the exponent of this theory believed that the amyloid bodies are a result of precipitation of the circulating fluids, (d) the hematogenic theory—a few workers thought that the amyloid bodies are the result of disintegrated blood elements, and (e) the 'post mortem' theory. Some workers believed that these bodies are merely the result of post-mortem change.

From the symptoms in this case and especially the terminal ones, it is difficult to believe that this pinhead nodular endothelial tumour was responsible for all the manifestations, i.e. extensive rash, sudden onset, a fit, unconsciousness and death. So the following conditions were thought of as possibilities in this strange

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MALARIA AT CHANDPUR (BENGAL)

By B. K. DAS

Malaria Inspector, Bird & Co., Bara Jamda

CHANDPUR is an important railway and steamer station in East Bengal, situated on the east bank of the river Meghna in the district of Tipperah. It is the only station connecting Calcutta with the Chittagong area and the Surma Valley of the Assam province.

The railway colony is situated on an angular projection between the rivers Meghna and Chandpur Khal, and is rather isolated from the town. Chandpur was for long known to be a healthy area, but during 1942, from July onwards, there has been a heavy outbreak of

(Continued from previous column)

symptom complex : (1) arsenical idiosyncrasy causing capillary dilation and increased capillary permeability of the brain, (2) arsenical encephalopathy, (3) chronic pulmonary tuberculosis with terminal broncho-pneumonia, and (4) German measles with post-measles encephalitis.

With regard to the fourth possibility, this diagnosis at first seemed to fit the case clinically, but was afterwards abandoned for several reasons. The rash in German measles rarely lasts more than 72 hours. In this case the rash lasted in a slight degree until death, i.e. 9 days after its appearance. There is a leucopenia in the eruptive stage of German measles, with a relative increase of lymphocytes. In this case, the total white cell count was 14,500 with 23 per cent of lymphocytes. The post-cervical glands all became markedly enlarged, but these glands enlarge with many infections, and in this case the possibility of the administration of arsenic stirring up latent tubercular or even syphilitic foci, had to be considered. Unfortunately a gland was not taken for section. In a case of encephalitis, one expects to find some cells in the cerebro-spinal fluid, but in this case there were none, nor did the histological examination of the brain show any characteristic picture. Finally, there were no other cases of German measles known to be in Calcutta at that time.

From all the available evidence, it seems reasonable to infer that the case was one of arsenical idiosyncrasy and encephalopathy with terminal broncho-pneumonia in a case of chronic pulmonary tuberculosis, the psammoma causing no symptoms and being a purely incidental finding.

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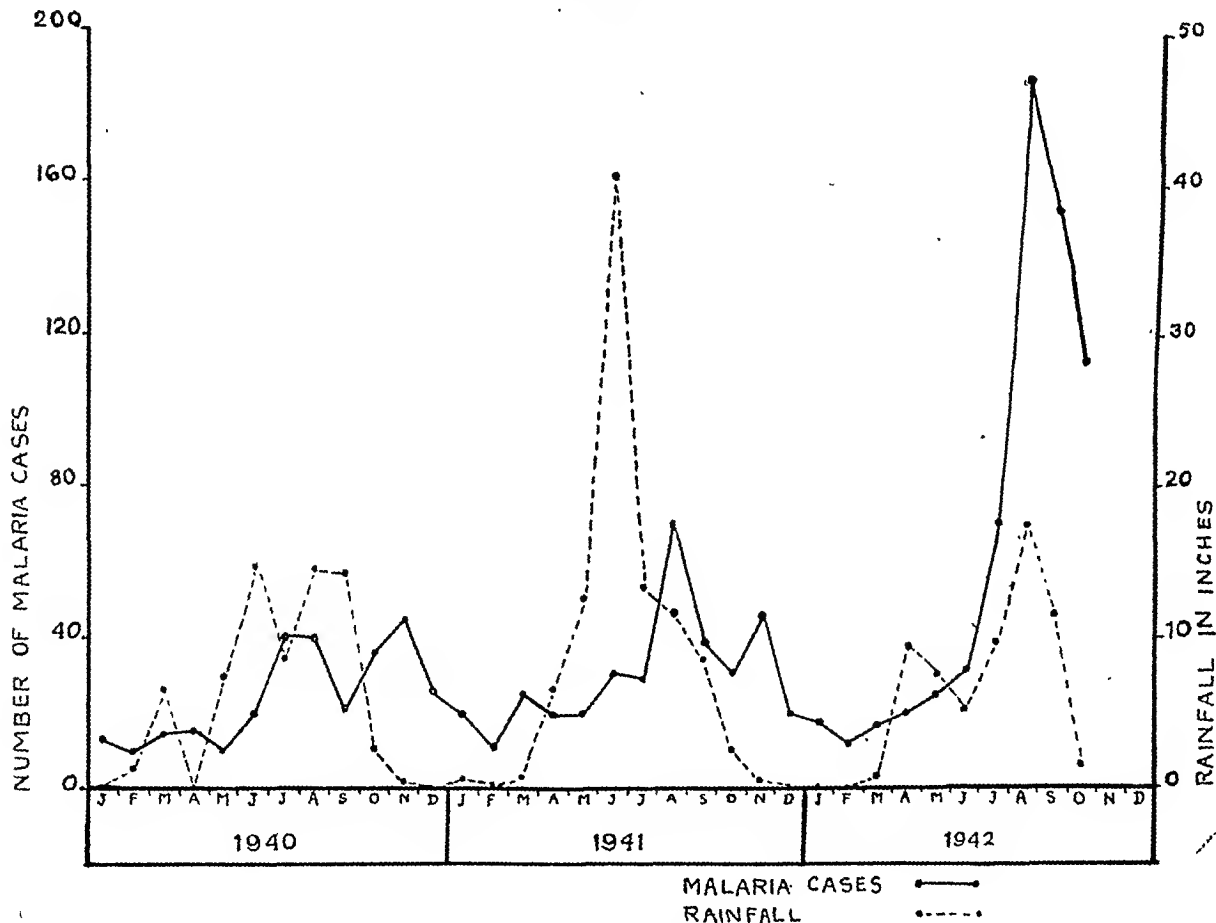
malaria. Messrs. Bird & Co. possess a small labour colony there, and the author was called to investigate, as the outbreak of malaria greatly hampered their business. The present paper is based on the results of a five-day survey (from 29th October to 2nd November, 1942) of the labour colony, which is situated within the railway colony of the B. & A. Railway. The labourers are recruited from various districts of Bihar and Orissa.

Though it is not possible to say definitely what caused the outbreak, the following seem to be contributory factors. During 1941 there had been very heavy rainfall—98.70 inches against 70.50 inches during 1940 (*vide* graph 1). This heavy rainfall prevented the normal drying up of many of the breeding places during summer, as a result of which, mosquito breeding continued during winter and summer, producing many more mosquitoes than normal. At this time of the year, a very large number of evacuees

opportunity to bite those carriers night after night, subsequently carrying the infection to the local people. When the rush of the evacuees declined, a large number of infected mosquitoes was left in the colony to infect the local population. This theory is supported by the fact that the outbreak of malaria was more severe in the railway colony than in the town. Another factor played a part in enhancing the process. There is less rainfall again in 1942 (65.44 inches up to October), associated by low tide water, which prevented the flooding of the breeding places and the flushing out of the water hyacinth, etc., from them, as happens almost every year. Consequently mosquito breeding continued uninterruptedly with increasing intensity. So the large number of infected mosquitoes was followed by a large number of infected people, who in turn infected larger number of fresh mosquitoes. Thus the whole process went on as in a vicious circle. Insufficient treatment of many of the

CHANDPUR BIRD'S DISPENSARY

Graph showing malaria cases and rainfall.



from Burma passed through the station, often staying for a night or two there, due to lack of accommodation in the steamers. It is quite probable that a large percentage of them were carriers of malaria, and in fact many of them had been suffering from fever. Now the large number of mosquitoes already present at the station, reinforced by the daily hatches, had the

patients due to shortage of quinine, and also due to negligence on the part of many of them, added more intensity to the process.

As is shown in graph 1, malaria cases began to increase from July and reached the peak in August. From the graph it seems that the cases were considerably less from September, but actually this is not the case. The daily attend-

ance of malaria cases was not on the decline at the time of the investigation. This graph includes only those patients who had never suffered before during the year, i.e., one man is recorded as a new case only once during the year; so all cases of reinfection are excluded from this graph. If it were possible to include the reinfections, the peak would have gone much higher and the decline would be much less rapid. This graph shows the figures of Messrs. Bird & Co.'s dispensary only. The records of the railway dispensary too show a marked increase of malaria (table I). There had been 527 cases of malaria in Bird's dispensary during

TABLE I

Showing number of malaria cases treated

Years ..	1940	1941	1942 (up to Oct.)
Railway dispensary	499	525	894
Bird's dispensary ..	288	361	641

the period July to October 1942, the time of the epidemic, against 169 during the same period in 1941; so the rise is actually to three times the normal.

Random samples of blood examined from the population showed a high percentage of infection and a very high gametocyte rate, as shown in table II. The high gametocyte rate is typical of epidemic conditions in an area of low endemicity.

are shown in table III. Though the number dissected is very small, the findings prove that *A. aconitus* is a carrier of first importance at Chandpur.

A. aconitus has so far not been considered as a carrier of any importance in this part of India. Senior White and Adhikari (1939) found only one gut infection in *A. aconitus* out of 48 (totalled from their tables II to VI) dissected around Chilka Lake, Orissa (Senior White and Adhikari, 1939). Covell and Pritam Singh recorded 674 dissections of *A. aconitus* in the Coastal Belt of Orissa without any infected specimen (Covell and Pritam Singh, 1942). In Assam 1,145 specimens of *A. aconitus* were dissected during the period 1931 to 1940, with only one gut infection (Viswanathan *et al.*, 1941). In Bengal, Iyengar recorded 1,494 dissections of this species, including 156 from Sitkund Thana of Chittagong district and 35 from Laksam Thana of Tipperah district, not far away from Chandpur, without finding any infected specimen. In this part of Bengal he found *A. philippinensis* as the vector (Iyengar, 1940). The author did not encounter any specimen of *A. philippinensis* either in the larval or adult stage at Chandpur. Though the search was confined to a limited area and to a short time, it seems from its absence that *A. philippinensis* is at least of secondary importance as a vector at Chandpur.

Out of 30 specimens of *A. aconitus*, 25 were caught from houses and 5 from slit trenches. The latter are made of brick lining with a roof of bamboo matting covered by grass, with a gap between the top of the trench and the roof. The

TABLE II

Result of random blood examinations

Number examined	Number positive	M. T.	B. T.	Mixed M. T. and B. T.	Crescents	Gametocyte rate
37	22	17	4	1	13	59.0%

Five species of anopheles were found breeding in tanks and borrowpits. They were: *A. aconitus*, *A. annularis*, *A. vagus*, *A. pallidus* and *A. hyrcanus*. Of these the first three were found in houses too. On dissection, only *A. aconitus* was found infected both in the mid-gut and in the salivary glands. The results of dissection

catches are shown in detail in table IV. *A. aconitus* constitute 27 per cent of the total females in the houses.

Five out of 12 big tanks and borrowpits searched showed larvæ of *A. aconitus* on a single search in each. They were chiefly among the roots of water hyacinth, even where its growth

TABLE III

Result of dissections

Species	Number dissected	Gut positive	Gland positive	Total infected	Sporozoite rate
<i>A. aconitus</i> ..	24	2	1	2*	4.1%
<i>A. annularis</i> ..	66

* One specimen had both gut and gland infections.

TABLE IV
Showing mosquitoes caught in houses and slit trenches

Species	IN HOUSES			IN SLIT TRENCHES			Total mosquitoes
	♂	♀	Total	♂	♀	Total	
<i>A. aconitus</i> ..	2	23	25	3	2	5	30
<i>A. annularis</i> ..	5	58	63	4	8	12	75
<i>A. vagus</i> ..	4	4	8	1	3	4	12

was so thick that the water surface was almost invisible.

The tanks, borrowpits and marshes with a heavy growth of various weeds including water hyacinth, constitute so big an area in and around the colony that anti-larval measures seem to be impracticable. Masses of water hyacinth are seen floating down the rivers, especially the Chandpur Khal, which probably will carry larvæ and pupæ from sources above and liberate some of them at the locality. This too may prove a serious handicap to the success of anti-larval measures. Further investigation is necessary before any scheme for anti-larval measures is adopted.

Summary

(1) The causes of a malaria epidemic at Chandpur railway and labour colony are discussed.

(2) *A. aconitus* is found to be the chief vector, with a sporozoite rate of 4.1 per cent. *A. philippinensis* seems to be of little or no importance, being conspicuous by its absence.

(3) The rôle of *A. aconitus* as a vector of malaria in Eastern India is discussed.

(4) The breeding places of *A. aconitus* are discussed.

(5) The prospects of anti-mosquito measures are discussed.

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ORO-GENITAL SYNDROME IN AVITAMINOSIS*

EFFECT OF TREATMENT WITH B₂ (COMPLEX) VITAMINS

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Introduction

ABOUT ten years ago, Fitzgerald (1932) suggested that a possible deficiency of vitamin B₂ in the diet, combined with consumption of irritant food and a state of weakened resistance of the digestive tract, might be responsible for an outbreak of 'exfoliative glossitis' associated with fissuring at the angles of the mouth in the jail population of this country. Later Nicholls (1934) reported the incidence of this particular labial lesion, i.e. angular stomatitis, along with phrynoderma in poorer school children and inmates of asylums in Ceylon. The existence of angular stomatitis amongst the prison population of the Malay Peninsula was reported by Landor and Pallister (1935) but with scrotal dermatitis added to the syndrome. Such findings were reported from other parts of the world also (Wright, 1936; Moore, 1937), and Stannus (1936) suggested that the oral syndrome was the earliest manifestation of pellagra. In this country, Aykroyd and his co-workers (1936 and 1939) and later Karunakaran and Nair (1940) have made serious attempts to study the ætiology of the syndrome by the therapeutic administration of protective foods such as skimmed milk, yeast powder, and soya bean, and drugs such as marmite and nicotinic acid. In the present investigation, an attempt has been made to find out the results of treatment of the oral and genital conditions referred to above, by the administration of two components of the B₂ complex, riboflavin and nicotinic acid, and also of some of the yeast and milk preparations.

* Being a paper read at the scientific section of the Bihar Provincial Medical Conference at Chapra, January 1943.

Experimental

In two residential institutions of this province, 32 boys between the ages of 12 and 18 years, and 59 adult males all above the age of 25 years, were selected from amongst 68 boys and 113 adults suffering from angular stomatitis, glossitis and/or scrotal dermatitis, for the investigation during the winter and spring of 1942, in four different batches. The first and the second batches consisted of 16 boys, and the third and the fourth batches consisted of 33 men and 26 men. Subjects with well-marked oral lesions (both labial and lingual) were selected for the enquiry, irrespective of the presence or absence of the scrotal condition. In the first batch and later in the second batch, boys were divided into groups of 4 for each kind of treatment, and an effort was made to distribute cases of the same degree of severity equally between all the four groups. Treatment was continued for 21 days or until recovery, whichever was earlier.

The lesions in the lips consisted of the usual erosion with a sodden appearance and cracks at the angles of the mouth. Facial dermatitis of the nature of the greasy desquamative lesion reported by American workers (Sebrell, 1942) in and around the nose, ears, eyes, etc., noticed in connection with the deficiency of B₂ complex, was not observed except in one of the boys who showed a fine scaly dermatitis in the nasolabial fold. In 2 other boys, an erosion of the prepuce was noticed.

The affection of the tongue was characterized by mild furring on the surface, tooth marking at the margin, fissures appearing all over, and flattening of papillae; in advanced cases either the whole of the tongue was purplish red or else covered with sharply defined patches caused by desquamation of the mucous membrane ('geographical' tongue).

The dermatitis in the scrotum was usually of the dry exfoliative type. At times the corrugations or rugae had disappeared, the skin presenting a smooth shiny appearance. In some cases, difficulty was experienced in stating definitely

whether the lesion of the scrotum was a part of the syndrome under investigation, or was caused by a specific infection. All doubtful cases have however been included.

A dietary survey covering a period of 10 days was carried out in both the residential institutions on the lines detailed in a previous communication from this laboratory (Mitra, 1940). The average daily intake per man-value consumption-unit (c.u.) of each class of foodstuff in ounces is shown in table I. In addition to the calorific value, an attempt has been made to make a rough estimate of the riboflavin content of the diets with the help of the table compiled by Swaminathan (1942). The cereals consisted of parboiled rice only in the institutions for boys, and of parboiled rice and wheat in the institutions for adults. The pulses consisted of red gram, lentil and Bengal gram, and the condiments of turmeric, chillies, coriander seeds and onion. It appears that the *per capita* intake of riboflavin in both the institutions fell far short of the daily requirements of 3 mg. worked out by Sebrell *et. al.* (1941). During the period under investigation, the subjects continued to be on their institutional diets.

Result of treatment given

I. *Shark liver oil*.—Each of the 4 boys in the first batch was given 0.25 oz. of shark liver oil daily. Each gramme of the oil was estimated to contain about 4,000 I.U. of vitamin A. Only very slight improvement was noticed in the first week of treatment in one of the subjects, but his condition showed no further improvement during the rest of the experimental period. Shark liver oil did not seem to have any effect on the syndrome.

II. *Skimmed milk*.—Each subject was daily given reconstituted milk in the shape of 1.5 oz. of skimmed milk powder, 'Acorn brand' imported from New Zealand, dissolved in 10.5 oz. of hot water. This treatment was given to 4 boys in the first batch and 4 adults in the fourth batch. The majority of the subjects were either

TABLE I
Different classes of food consumed by the subjects

Classes of food	Boys		Adults	
	Consumption in ounces per c.u.	Approximate riboflavin content μ g.	Consumption in ounces per c.u.	Approximate riboflavin content μ g.
Cereals	17.7	402	19.0	602
Pulses	3.7	158 to 315	6.0	255 to 511
Leafy vegetables	0.9	12
Non-leafy vegetables	6.0	34 to 172	6.0	34 to 172
Vegetable oil	0.3	..	0.6	..
Condiments	0.4	..	0.25	..
Fruits	1.0	28
Total calories	2,324	606 to 901	3,174	919 to 1,313

TABLE II—(First batch)

16 boys

Clinical condition	Number under treatment	Slight improvement	Marked improvement	Cured	No change	Medicine used and daily dosage	REMARKS
Angular stomatitis ..	4	1	3	Shark liver oil 0.25 oz. daily.	
Glossitis ..	4	4		
Scrotal dermatitis ..	2	2		
Angular stomatitis ..	4	2	2	Nicotinic acid tablets 150 mg. daily.	In every case slight relief from the burning sensation in the tongue was reported.
Glossitis ..	4	2	1	..	1		
Scrotal dermatitis ..	4	2	2		
Angular stomatitis ..	4	4	..	Skimmed milk powder 1.5 oz. and hot water 10.5 oz. daily.	
Glossitis ..	4	..	2	2	..		
Scrotal dermatitis ..	4	..	2	2	..		
Angular stomatitis ..	4	4	..	Lactoflavin tablets 5 mg. daily.	One patient with affection in naso-labial fold was cured.
Glossitis ..	4	..	2	2	..		
Scrotal dermatitis ..	2	..	1	1	..		

cured, or there was marked improvement in their clinical condition. In one subject the improvement noticed at the angle of the mouth was not striking.

brewer's yeast. Sometimes a small quantity of cane sugar was mixed with the powder, to make it palatable. Slight improvement was observed in about 8 to 10 days in 2 cases, and

TABLE III—(Second batch)

16 boys

Clinical condition	Number under treatment	Slight improvement	Marked improvement	Cured	No change	Medicine used and daily dosage	REMARKS
Angular stomatitis ..	4	2	1	1	..	Brewer's yeast 1 oz. daily.	One case with affection of prepuce was cured.
Glossitis ..	4	2	1	1	..		
Scrotal dermatitis ..	3	1	2		
Angular stomatitis ..	4	1	3	Nicotinic acid 150 mg. daily.	Oral and scrotal condition aggravated in one case.
Glossitis ..	4	2	2		
Scrotal dermatitis ..	1	1		
Angular stomatitis ..	4	4	..	Lactoflavin tablets 5 mg. daily.	One case with affection of prepuce was cured.
Glossitis ..	3	..	1	2	..		
Scrotal dermatitis ..	3	..	2	1	..		
Angular stomatitis ..	4	4	..	Lactoflavin 3 mg. and nicotinic acid 100 mg. daily.	
Glossitis ..	3	3	..		
Scrotal dermatitis ..	2	2	..		

III. *Dahi* (curdled milk).—To each of the 10 persons of this group, curdled milk prepared from 1 lb. of fresh whole cow's milk was given daily. Boiled whole milk was not tried; the majority of the subjects were poor class people and could not remember having drunk milk for a long time; it was apprehended that liquid whole milk might not have suited some of them; moreover the subjects themselves preferred *dahi* to boiled milk. Out of 10 subjects under treatment, 7 were completely cured.

IV. *Dried brewer's yeast*.—Four boys of the second batch were given daily 1 oz. of dried

one case was completely cured; marked improvement was noticed in the fourth.

V. *Handia yeast*.—The aborigines in this province ferment their country liquor with rice grains. The spent rice grains from their earthenware fermenting vats were collected, dried in the sun, and powdered, but the dried powder was found to possess a slightly unpleasant smell and taste. It was tried on 7 adult persons only, with a dosage of an ounce daily, and all that can be said is that the results were not discouraging. The peculiar

smell and taste of the powder prevented its use in larger dosage.

VI. *Liquid yeast*.—This was a mixture of white flour and sugar incubated with yeast at 27°C. (inside an incubator) in an enamelled iron mug. After 24 hours, the fermented mixture developed the look of custard with a pleasant taste and flavour. A small quantity of this 'liquid yeast' was used as the 'seed' for fer-

menting the successive brews in the proportion:—

Flour	4 oz.
Sucrose	4 oz.
Liquid yeast	2 oz.
Water	2 oz.

Two tablespoonfuls (roughly equivalent to 46 g.) of the preparation were given daily to 10

TABLE IV—(Third batch)

Adults

Clinical condition	Number under treatment	Slight improvement	Marked improvement	Cured	No change	Medicine used and daily dosage	REMARKS
Angular stomatitis ..	4	..	1	3	..	Lactoflavin 2 mg. injection daily.	One case relapsed after 22 days.
Glossitis ..	4	4	..		
Scrotal dermatitis ..	4	..	2	2	..		
Angular stomatitis ..	6	..	1	5	..	Lactoflavin 5 mg. (oral) daily.	
Glossitis ..	6	..	1	5	..		
Scrotal dermatitis ..	5	5	..		
Angular stomatitis ..	3	2	1	Handia yeast 1 oz. daily.	
Glossitis ..	3	1	2		
Scrotal dermatitis ..	3	1	1	..	1		
Angular stomatitis ..	10	2	3	5	..	Liquid yeast 2 spoonfuls daily.	
Glossitis ..	10	5	2	3	..		
Scrotal dermatitis ..	4	1	2	1	..		
Angular stomatitis ..	10	2	1	7	..	Dahi or curdled milk 1 lb. daily.	
Glossitis ..	10	2	1	7	..		
Scrotal dermatitis ..	5	1	1	2	1		

TABLE V—(Fourth batch)

Adults

Clinical condition	Number under treatment	Slight improvement	Marked improvement	Cured	No change	Medicine used and daily dosage	REMARKS
Angular stomatitis ..	4	2	2	Handia yeast 1 oz. daily.	
Glossitis ..	4	2	1	..	1		
Scrotal dermatitis ..	2	2		
Angular stomatitis ..	6	3	2	..	1	Liquid yeast 2 spoonfuls daily.	
Glossitis ..	6	3	2	..	1		
Scrotal dermatitis ..	4	2	1	..	1		
Angular stomatitis ..	4	1	1	2	..	Skimmed milk powder 1.5 oz. and hot water 10.5 oz. daily.	
Glossitis ..	4	..	2	2	..		
Scrotal dermatitis ..	2	..	1	1	..		
Angular stomatitis ..	4	1	3	Nicotinic acid 150 mg. daily.	Oral and scrotal condition aggravated in one case.
Glossitis ..	4	2	2		
Scrotal dermatitis ..	2	1	1		
Angular stomatitis ..	4	4	..	Lactoflavin 5 mg. by mouth daily.	
Glossitis ..	4	4	..		
Scrotal dermatitis ..	4	1	..	3	..		
Angular stomatitis ..	4	1	1	2	..	Lactoflavin 2 mg. injection daily for 12 days.	
Glossitis ..	4	1	1	2	..		
Scrotal dermatitis ..	3	3	..		

adults in the third batch, and to 6 adults in the fourth batch. The results were encouraging in both the batches, though the group under treatment in the third batch gave more favourable results than those in the fourth batch.

The approximate potency of riboflavin and nicotinic acid in the different milk and yeast preparations used is shown below. The estimations have all been carried out in Nutrition Research Laboratories, Coonoor. For unavoidable reasons the potency of the liquid yeast could not be estimated.

TABLE VI

Approximate riboflavin and nicotinic acid content of the milk and yeast preparations

	Riboflavin μg./g.	Nicotinic acid μg./g.
Skimmed milk powder ..	16.0	10.0
Dahi* ..	2.0	1.0
Brewer's yeast ..	40 to 50	400 to 500
Handia yeast ..	23.2	90.0

* Calculated from figures for fresh whole milk.

VII. *Nicotinic acid tablets*.—A daily dose of 3×50 mg. tablets of nicotinic acid was administered to 8 boys and 4 adults. A little more than half showed no change. One remarkable feature was that no less than 6 persons seemed to respond to the treatment at about the end of the first week, but the slight progress noticed did not continue. The main improvement noticed was slight relief in the burning sensation of the tongue. In one boy in the second batch and one adult in the fourth batch however, the lesions in the lips and scrotum seemed to grow worse during the course of the treatment. One of the boys under treatment complained of headache and vague pains in the limbs, and one adult complained of a sensation of warmth in the abdomen some time after the administration of the dose. In both the cases, the sense of discomfort did not last for more than 2 hours.

VIII. *Riboflavin**.—Each of the 8 boys and 10 adults were given daily 5×1 mg. tablets of 'Lactoflavin' (Roche) by mouth, and the result reported leaves very little to be desired. All the subjects under treatment were either cured completely or else showed marked improvement. The action of this synthetic drug on the course of the clinical manifestations was so effective that the other groups under treatment clamoured for this particular preparation. In 2 of the boys, the glossitis persisted in a mild form even after three weeks' treatment with riboflavin, and

the improvement was comparatively slow. A rapid cure was obtained in both these cases, within 3 to 5 days by a combined administration of 3 mg. riboflavin and 100 mg. of nicotinic acid per day. Cure was usually effected in from 12 to 17 days.

To 8 persons lactoflavin in solution was administered parenterally. The daily dose was 2 mg. per subject. In 8 to 12 days' time, the oral lesions disappeared completely in 5 persons, 2 showed marked improvement, and in one case the improvement was slight; of these 8 subjects 7 were suffering from scrotal complications of which 5 were completely cured and the remaining 2 were almost cured. One of the subjects in this group reported a recurrence of his labial lesion three weeks after the treatment had been discontinued.

IX. *Riboflavin and nicotinic acid*.—With a view to finding out whether riboflavin acted more efficiently in combination with nicotinic acid, 3×1 mg. of lactoflavin (Roche) and 2×50 mg. of nicotinic acid in tablet form were administered daily to 4 boys in the second group. In all the four cases the lesions disappeared completely by the 18th day. Two boys of the riboflavin group were also given this combined treatment with success as stated previously.

Discussion

From the results of the present study it is evident that the *oro-genital syndrome** can be cured or relieved by the administration of preparations rich in the vitamin B₂ complex. Of the different preparations tried, synthetic riboflavin proved to be of great value in the cure of the clinical manifestations in the lips, tongue, prepuce and scrotum. Under riboflavin treatment, the physical signs and the subjective symptoms, e.g. pain, burning sensation, itching, etc., either disappeared or else markedly improved. In a few cases however, another synthetic B₂ preparation, nicotinic acid, seemed to act as a very suitable adjunct to riboflavin. Vilter, Vilter and Spies (1939) were of the opinion that pellagrous dermatitis in patients treated with nicotinic acid could be cured quickly if riboflavin was administered. In the present study, the number of cases under treatment has been too small to justify any conclusion on this point.

The curative value of nicotinic acid alone in this syndrome, though reported by Katzenellenbogen (1939), Aykroyd *et al.* (1939) and Manson-Bahr (1941) could not be confirmed in the present study. Spies *et al.* (1938) were sceptical as to the efficacy of nicotinic acid alone on the course of the syndrome, and Landor (1939) reported that his cases did not respond to nicotinic acid. More recently Duckworth (1942) has reported failure to cure 2 chronic cases suffering from this syndrome every winter by

* The commercial name 'Lactoflavin' of this particular preparation used, has been retained in the tables but the more correct terminology riboflavin (this compound owes its activity to the presence of d-ribityl molecule at position 9 of the iso-allaxozine ring) has been preferred in the text.

* The term *oro-genital syndrome* was coined by Nair (*J. Indian Med. Assoc.*, 1939, Vol. 8, p. 215) to designate the clinical conditions under review.

nicotinic acid alone; his cases being finally cured by the administration of riboflavin. Sydenstricker, *et al.* (1939) have reported that, of their series of 5 cases, 4 were cured with riboflavin, and the fifth by parenteral administration of nicotinic acid combined with a 'soft pellagra-curative diet'. In this particular case, there was a dramatic response of the glossitis and stomatitis to nicotinic acid treatment. By the third day, the condition was much improved, and by the fifth day the cheilitis had disappeared. The authors have tried to explain, not very convincingly, that the patient became greedy after the first day of treatment and consequently she consumed foods rich in riboflavin in the soft pellagra-curative diet, the details of which have not been given. In the present series, with nicotinic acid alone, some alleviation of the subjective symptoms and clinical signs was noticed in a few cases during the first week of treatment, but the improvement stopped, and in two of the subjects who did not respond, the condition seemed to deteriorate after 10 days' treatment. It is very difficult to hazard any opinion as to whether the deterioration in their condition was due to natural causes or to nicotinic acid precipitating ariboflavinosis (Sydenstricker, 1941a).

The reason for these apparent anomalies and contradictions with regard to the action of nicotinic acid on angular stomatitis and glossitis is not far to seek. Some of the manifestations of the present-day ariboflavinosis formed for a very long time a part of the symptom-complex of classical pellagra. The confusion existing in the earlier literature concerning the physical and subjective manifestations of lack of the vitamin B₂ complex has been clarified to a certain extent by the identification of nicotinic acid as the pellagra preventive factor, and the elucidation of the clinical signs of human ariboflavinosis, notably by Sebrell and Butler (1938 and 1939); but some wide gaps in our knowledge on the subject remain yet to be filled up.

The present knowledge on ariboflavinosis can be summed up under two broad heads, clinical and physiological.

(1) *Clinical*.—Angular stomatitis (cheilitis of American workers), a specific type of glossitis, seborrhœal affections of the facial skin, particularly in the neighbourhood of ear, eye and nose, scrotal dermatitis and whitish looking erosions of the prepuce and vulva, and some forms of ocular lesion can be cured by the administration of riboflavin. It has not, however, been established with any degree of precision whether better clinical results would follow in some of the cases if riboflavin be supplemented by the addition of nicotinic acid or pyridoxine (vitamin B₆) or any of the other factors of the vitamin B₂ complex.

(2) *Physiological*.—Riboflavin is the reactive constituent of the flavo-protein or yellow ferment of Warburg (coenzyme factor), and is present presumably in all living cells as a component of

an oxidation enzyme which is used up in the cellular respiration, and consequently has to be replaced from outside. This coenzyme factor is responsible for the fractional dehydrogenation (equivalent to oxidation) of coenzymes I and II, and itself gets reduced in the process. The coenzymes I and II are diphosphopyridine and triphosphopyridine nucleotides, and nicotinic acid is their active constituent. The coenzymes I and II in their turn are necessary for the fractional dehydrogenation of some of the intermediate products of carbohydrate metabolism, and themselves get reduced during the process and are oxidized by coenzyme factor. The reduced 'coenzyme factor' regains its oxygen, possibly through cytochrome and indophenol oxidase. The coenzymes (I and II) and the coenzyme factor, *i.e.* nicotinic acid-containing enzyme and riboflavin-containing enzyme, are essential for metabolism of hexoses in the human organism.

Some workers are inclined to believe that in subjects whose nutrition balance is in some way imperfect (in other words, the capacity of this particular enzyme system for the oxidation-reduction process is poor, though adequate at a given level) the equilibrium is apt to be upset if any new factor such as hard work, incarceration, indulgence in alcohol or even parenteral administration of glucose, is introduced, leading to an increased rate of metabolism and resultant depletion of any one of the enzymes in the chain. If the limiting factor happens to be coenzymes I and II, the resultant clinical condition can be cured by the administration of nicotinic acid, and if the 'coenzyme factor' fails, then the administration of riboflavin cures the deficiency syndrome. It is not difficult to imagine conditions in which both the factors may be at fault.

This justifiable speculation explains the conflicting experience of nicotinic acid therapy in the hands of different observers, and its apparently supplementary effect with riboflavin; but it certainly does not explain why imperfect oxidation or dehydrogenation of intermediate metabolites leads to specific lesions in lips, tongue, eye, scrotum, etc. Again, why is it that in one set of persons the ocular manifestations prevail in preference to the oral and perineal lesions, and in others the oro-genital signs and symptoms predominate with apparently nothing abnormal in the eye? In the present group of 91 subjects under investigation, the eye symptoms were conspicuous by their absence. It is admitted that by naked eye examination alone, mild cases of keratitis might have been missed, but all the subjects in the present series were definite that none of them were suffering from the burning sensation in the eye, photophobia or lachrymation so characteristic of the ocular lesion in ariboflavinosis. Sydenstricker (1941b) has stated that in more than half the cases of ariboflavinosis examined by him, the ocular symptoms have preceded all others. In this country also, Aykroyd and Verma (1942) have

come across a considerable number of cases of the oro-genital syndrome associated with ocular manifestations. Stannus (1940) has very pertinently observed that he had found it difficult to believe that 'nature has provided a special vitamin to ensure the welfare of a few centimeters of skin'. Only further intensive work can clarify the position.

Of the other curative substances used, there is very little to say. The milk preparations, e.g. re-constituted skimmed milk and fermented milk or *dahi*, owing to their high B₂ complex content, gave the anticipated results. The curative effect of yeast also has been proved by previous workers. The various yeast preparations were tried with a view to comparing results and also to exploring the possibility of devising some cheap and effective remedy for the syndrome which is fairly common in certain parts of this province (Bihar). From the results of these experiments, it can be justifiably concluded that had the indigenous preparations of yeast been administered in larger doses, a higher cure rate could have resulted. Landor and Pallister (1935) reported very favourable results when only 4 oz. of fresh brewer's yeast were daily administered to each of the cases. The cheapest of the three yeast preparations used, the spent rice grains from vats of country liquor, *handia*, was found to be least effective, though it was found to be a moderate source of B₂ vitamins. This particular preparation could not be used in larger doses, as it retained the unpleasant smell and taste even after drying in the sun, probably due to the presence of undesirable organic acids.

Summary

Thirty-two boys and fifty-nine adult males suffering from a syndrome consisting of angular stomatitis, glossitis and scrotal dermatitis were treated in batches by the administration of milk and crude yeast preparation and also with synthetic riboflavin and nicotinic acid.

Under oral or parenteral administration of synthetic riboflavin, the clinical manifestations disappeared completely in about three weeks' time. Nicotinic acid alone was found to be of insignificant value. The impression of the author has been that, in some of the cases, nicotinic acid has acted as a suitable adjunct to riboflavin. The possible aetiology of the oral and other lesions comprising the syndrome has been discussed.

Acknowledgment

The author is grateful to Messrs. Hoffman La Roche for the free supply of 'Lactoflavin' (Roche) tablets and ampoules used during the investigation, and to his chief Rai Bahadur Dr. B. P. Mozoomdar, Director of Public Health, Bihar, for his encouraging interest in the work.

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(Concluded at foot of next column)

A. COMPLEMENT-FIXATION TEST FOR KALA-AZAR

By P. C. SEN GUPTA, M.B. (Cal.)

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COMPLEMENT-FIXATION tests have, at the present time, been devised for various bacterial, protozoal and metazoal diseases, and for the identification and differentiation of such substances as serum, blood, milk, etc. Attempts had been made in the past to devise a complement-fixation test for kala-azar by the Italian workers Pavoni, Cristina and Caronia, but these did not prove very successful (Brahmachari, 1928). It seems probable that the Italian workers used some antigen prepared from the leishmania and the reaction they obtained was apparently not of a high order and was positive in only a small proportion of cases of kala-azar.*

* Recently Niyogi and Ray (1942) have reported a positive complement-fixation reaction in a small series of cases of kala-azar with the use of antigen prepared from cultures of leishmaniae.

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It is a very curious fact that, in the complement-fixation test which we propose to discuss in this paper, the antigen that is used is of an entirely different nature, and was originally prepared for an entirely different purpose.

The antigen referred to is that of Witebsky, Klingenstein and Kuhn, prepared from the human tubercle bacillus. It is essentially the alcohol insoluble, pyridin soluble, acetone insoluble fraction of the tubercle bacillus in benzolic solution with lecithin added.

This antigen was originally prepared for complement-fixation test in the diagnosis of tuberculosis, but the results have been poor. It was tried by South American workers and later in India by Lowe and Greval (1939) in leprosy. The results were interesting, but not of much practical value, the positive reaction being confined to those cases in which ordinary clinical and bacteriological diagnosis was easy. A standardized technique was devised by Greval, Lowe and Bose (1939).

Bier (quoted by Lowe and Greval) was apparently the first to record a positive reaction in 70 per cent cases of leishmaniasis in South America. Lowe and Greval (*loc. cit.*) confirmed the result in Indian kala-azar; positive results were obtained in all the 17 cases of kala-azar tested and in 1 out of 3 cases of dermal leishmaniasis. They used a serum dilution of 1 : 5. Greval, Lowe and Bose (*loc. cit.*) tested the titre of some pooled serum of kala-azar patients and found a positive reaction in 1 : 25 dilution of serum and doubtful reaction in 1 : 50 dilution. The subject of complement fixation in Indian kala-azar was further worked out (Greval, Sen Gupta and Napier, 1939) at the Calcutta School of Tropical Medicine. The technique was slightly modified, *viz.*, in using higher serum dilutions, 1 : 25, 1 : 100, than that used in leprosy by Greval, Lowe and Bose, and it was found that the reaction was positive in all proved cases of kala-azar, and that it possessed a diagnostic value of high order.

The writer, who had been concerned with the serological investigation and the correlation of the results with clinical data, continued the work after the publication of the above paper (Greval, Sen Gupta and Napier, *loc. cit.*), and collected the relevant data regarding a large series of cases. In this paper, it is proposed to set forth the results of the complement-fixation test with W.K.K. antigen done so far by him (including those already published) and to discuss the value of this test in the diagnosis of kala-azar. The effect of treatment on this reaction will also be described.

As for the test itself, it is unnecessary to describe the details of technique and the mode of preparation of the antigen as these have already been given elsewhere (Greval, Sen Gupta and Napier, *loc. cit.*; Greval, Das and Sen Gupta, 1941). It will be enough to mention that, in the complement fixation with W.K.K. antigen for kala-azar, the following are used : (a)

the hæmolytic system of method no. 4 of the Wassermann test of the Medical Research Committee (1918), (b) the maximum quantity of antigen not interfering with 1 m.h.d. of complement, and (c) 1 : 25 and 1 : 100 dilutions of serum. In this test the dose of complement (2 m.h.d.) is kept fixed, and dilutions of serum are varied; this is done for two reasons, *viz.*, that less complement is needed, and that the differences in complement fixation in general are brought out better by decreasing the serum than by increasing the complement. The serum dilution of 1 : 25 was adopted, instead of the usual 1 : 5 (as in the Wassermann reaction) as the lowest significant dilution, because at this dilution it was found that other diseases (except leprosy) give negative results. Also, only complete complement fixation (*i.e.* a + reaction) is to be regarded as positive and others including doubtful reactions (T, ±, ? -) as negative. Only in very early cases with a small spleen are those minor degrees, T or ± reaction, of complement fixation to be looked upon with suspicion, and the test subsequently repeated.*

Analysis of the results of the complement-fixation test

Table I gives a summary of the results of the complement-fixation test with W.K.K. antigen in a series of 434 cases; it will be seen that of 177 cases diagnosed as kala-azar, 172 (97 per cent) gave a positive result. The result was negative in a large series of controls consisting of (i) 176 cases referred to the kala-azar clinic of the Calcutta School of Tropical Medicine, on suspicion of kala-azar, *viz.*, the cases of chronic malaria, splenic anæmia, splenomegaly, enteric fever, etc., in which kala-azar was excluded by serum tests and parasitological examination done whenever deemed necessary, (ii) 50 cases from the wards of the Carmichael Hospital for Tropical Diseases consisting of various febrile diseases such as malaria, enteric fever, pulmonary tuberculosis, dengue, hepatitis, pleurisy with effusion, etc., afebrile or low pyrexial conditions such as anæmia, diabetes, drug addiction, dysentery, amœbiasis, colitis, splenomegaly, etc. The sera of 25 cases of chronic pulmonary tuberculosis were tested, and in only 1 case, a very chronic case, afebrile and apparently progressing favourably was the test positive.

Discussion

From the above account and from table I, it will be evident that a complement-fixation test

* The results of complement-fixation tests are read as follows :—

Complete inhibition of lysis ..	+	= positive.
A trace of lysis ..	T	} = doubtful.
More than a trace of lysis ..	±	
Lysis almost complete, only turbidity present, no coloured deposit	? -	} = negative.
Lysis complete ..	-	

has been evolved that possesses a high degree of 'specificity' for kala-azar. Other than severe leprosy which can easily be excluded, all other diseases likely to be considered in the differential diagnosis of kala-azar give a negative result. In only 1 out of 25 cases of pulmonary tuberculosis a positive result was obtained, and in the rest the result was negative. It is thus reasonable to conclude that a patient not suffering from leprosy or dermal leishmaniasis (in which condition some positive results are obtained) whose serum gives a positive result in this test is almost certainly suffering from kala-azar.

It will be seen that in 21 out of 22 cases of parasitologically diagnosed kala-azar, in which the aldehyde test was doubtful or negative, the complement-fixation test gave a positive reaction. It is thus evident that the test becomes positive earlier than the aldehyde test. It is difficult to determine exactly when in the course of kala-azar the test becomes positive. The history of duration of illness is usually very unreliable; the splenic enlargement often serves as a better guide. In the whole series of cases of kala-azar in which the test was carried out, the shortest duration of illness before the test was done (and a positive reaction obtained) was about four weeks.

Case note

P. C. B., a Bengalee male, aged 34 years, was admitted on the 13th November, 1938, for continued fever since 24th October, 1938. On admission the patient had a temperature of 102°F. The liver was just

palpable and the spleen enlarged to about 1 inch below the costal margin. No other abnormality was detected. The aldehyde and the antimony tests were negative. Sternal puncture did not show any leishmania. The complement-fixation test was done on the 25th November, 1938, and was found to be positive. Spleen puncture done on 6th December, 1938, showed leishmania.

It would thus appear that the reacting antibody responsible for this complement-fixation reaction, appears very early in the course of the disease. The shortest duration of illness with a positive complement-fixation test has been found so far to be about four weeks. This is much earlier than the appearance of positive reaction in the antimony or the aldehyde test. Further work on early kala-azar will no doubt throw more light on this point, *viz*, exactly when the reaction becomes positive; but from the present work, it appears that, apart from a sternal puncture or a difficult spleen or liver puncture (there being usually slight enlargement of the organs at the early stages of kala-azar), this test enables an earlier diagnosis of kala-azar to be made than other tests.

Effect of treatment on the complement-fixation test

Table II gives the results of the complement-fixation test in 22 cases before and after treatment. In 11 cases a positive reaction changed to negative (including two doubtful reactions as negative); in 6 cases there was a distinct fall in titre of the reaction as judged by the degree of

TABLE I
Complement-fixation test with W.K.K. antigen

	Number of cases	SERUM DILUTION 1:25			SERUM DILUTION 1:100			REMARKS
		Negative	Doubtful	Positive	Negative	Doubtful	Positive	
I. Kala-azar cases 227								
1. Aldehyde positive, parasitological examination deemed unnecessary.	50*	Nil	Nil	50	Nil	Nil	6	1:100 dilution not tested in 44 cases. 8 negative in 1:100 dilution include 4 that showed \pm reaction in 1:25.
	100	Nil	4	96	8	28	64	
2. Parasite positive, aldehyde negative.	7	1	Nil	6	1	2	1	1:100 dilution not tested in 3 cases.
3. Parasite positive, aldehyde doubtful.	15	Nil	Nil	15	1	3	11	
4. Clinically diagnosed, aldehyde doubtful, responded to treatment.	5	Nil	Nil	5	Nil	3	2	
II. Controls								
1. Pulmonary tuberculosis .. ?K.A. (aldehyde test +++)	25	23	1	1	—	1	—	1:100 dilution not tested in rest of the cases.
+ pulmonary tuberculosis.	1	—	—	1	—	1	—	
2. Dermal leishmaniasis ..	5	1	3	1	4	1	Nil	
3. Miscellaneous diseases other than kala-azar and leprosy.	226	214	12	Nil	226	—	—	

* Previously reported.

TABLE II

Effect of treatment on complement-fixation test with W.K.K. antigen in kala-azar (22 cases).

Case number	RESULT OF COMPLEMENT-FIXATION TEST IN SERUM DILUTION				Case number	RESULT OF COMPLEMENT-FIXATION TEST IN SERUM DILUTION			
	Before treatment		After treatment			Before treatment		After treatment	
	1 : 25	1 : 100	1 : 25	1 : 100		1 : 25	1 : 100	1 : 25	1 : 100
1	+	T	-	-	12	+	T	-	-
2	+	T	-	-	13	+	+	+	±
3	+	T	T	? -	14	+	+	+	±
4	+	T	+	+	15	+	+	+	-
5	+	-	? -	+	16	+	+	-	-
6	+	+	+	-	17	+	±	-	-
7	+	+	+	+	18	+	..	-	..
8	+	+	+	+	19	+	..	T	..
9	+	T	+	±	20	+	..	+	..
10	+	+	+	T	21	+	..	+	..
11	+	+	-	-	22	A.C.	..	A.C.	..

A.C. = Anti-complementary.

fixation in 1 : 100 dilution of serum; in 4 cases there was no apparent serological change, and in 1 case the serum was anti-complementary both before and after treatment. It would thus appear that the general tendency of the reaction is to become negative as a result of the patient recovering after treatment. The reaction thus may serve as a guide to cure of the disease.

Summary

Analysis of the results of a complement-fixation test using the Witebsky, Klingenstein and Kuhn antigen according to a technique described by Greval, Sen Gupta and Napier (*loc. cit.*) in a series of 434 cases has shown that with this technique using 1 : 25 and 1 : 100 dilutions of serum, a complement-fixation reaction is obtained in 97.1 per cent of cases of kala-azar. The reaction becomes positive very early in the course of kala-azar, the shortest duration of illness with a positive reaction being four weeks. The results of the test done before and after a course of treatment in a small series of cases, show that the reaction tends to become negative as the patient recovers.

The test is apparently highly 'specific' for kala-azar, being negative in all diseased conditions likely to be considered in the differential diagnosis of kala-azar.

Acknowledgment

The serological investigations were carried out by the writer in the laboratory of the Imperial Serologist (Lieut.-Colonel S. D. S. Greval, I.M.S.) and the kala-azar cases investigated were under Dr. L. Everard Napier. The writer expresses his thankfulness to Colonel Greval and Dr. Napier for help and encouragement.

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X-RAY TRACING: A SUBSTITUTE IN FILM SHORTAGE

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If films are not available, x-ray examination is restricted to fluoroscopy (screening). Screening reports, always tiresome to read, may fail to convey the examiner's genuine impression of the fluoroscopic picture. The physician or surgeon reading reports, and even the radiologist looking up previous reports, may not fully grasp their significance. Many doubts and misunderstandings can be obviated, if the report is supported by a tracing which is able, to a certain extent, to replace a film. The technique is very simple and can be performed by every x-ray examiner. The procedure developed by our tuberculosis section is as follows:—

1. An old or spoiled film is washed clean and made transparent. (Blue tinted films are not recommended as they are apt to dim the fluoroscopic contrasts.)

2. The film, thus prepared, is placed before the screen, and the essential fluoroscopic outlines

(Concluded on next page)

TREATMENT OF UNDULANT FEVER WITH SULPHANILAMIDE

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and

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THE remedies advocated for the treatment of undulant fever are numerous and varied; this has naturally led to the view that none is really effective. The vaccines have proved of limited use; they often give rise to severe reaction, especially when given intravenously, and the beneficial effect is perhaps largely due to protein shock. When trypanflavin was introduced, great hopes were entertained, and good results were claimed; the same may be said of mercurochrome, and of foudadin, a trivalent antimony preparation, but none was established as a really effective therapeutic agent. Recently claims have been made regarding the efficacy of the sulphonamide group of drugs in the treatment of undulant fever, but the reports are so far conflicting. The note below describes a case of undulant fever treated with the more recent

(Continued from previous page)

and shadows are traced upon it with a skin pencil. It goes without saying that the patient, the screen and the tube should be fixed beforehand in the required position, and that none of them should be displaced during the act of tracing.

3. A thin transparent tracing paper is laid over the film tracing, and both are put before a window pane or an x-ray viewer if available. The markings of the film tracing are then copied upon the paper.

The film may be washed and used again. It is convenient to keep several films ready for a sitting of more than one screening.

Every x-ray examiner, with practice, can acquire increasing skill in rendering qualitative details of linear, nodular, homogenous, confluent, cavity shadows, etc. The same applies to marking the outlines after barium meals in abdominal fluoroscopy, as well as to recording fractures and dislocations of bones. Pathological features of bone and joint structure, however, which are hardly discernible in screening, are unsuitable for tracing.

Some x-ray plants have a contrivance for putting cellophane sheets before the screen, originally meant for orthodiagraphy of the heart. By this method, of course, the second act of copying is unnecessary. As however cellophane sheets may also not be available, the x-ray examiner may have recourse to the x-ray tracing here recommended.

For his ready help and facilities offered, my thanks are due to Dr. V. P. Trivedi, M.B., B.S., in charge of our X-ray Department.

compounds of the drug, a case which is of interest not only because it afforded an opportunity to observe their effects, but also because of the rarity of this disease in this country.

It is however possible that the disease is more prevalent than it is generally supposed. These considerations justify, we hope, the publication of the following case report:—

A Bengali Hindu male, an office worker, aged 26 years, was admitted to the Carmichael Hospital for Tropical Diseases on 28th March, 1941, complaining of fever without remission for eight days.

History.—On 31st December, 1940, the patient felt extremely tired in the evening, so that he remained indoors. On the following morning he had severe headache with no inclination for food; he however carried on his usual work. Next day, while in the office, he felt very uneasy, and the headache was so severe that he had to return home.

His temperature went up to 100°F., and he had severe pains all over the body, as well as a slight cough. A doctor was called, who attributed the condition to an influenzal attack. The fever (of remittent type), however, persisted. The maximum temperature (103.8°F.) was reached about the fourteenth day of illness, and then it gradually subsided being normal about the twenty-fifth day of illness. He was treated as a case of enteric fever. He resumed his office work on 2nd February. After a few days he lost his appetite and felt weak and unusually tired especially towards the evening, although he continued to attend his office. Thereafter, he developed fever with occasional chilly sensations. He used to sweat profusely at times and also had pains in the body, worse at night, with disturbance of sleep. He began to lose weight steadily; tuberculosis was suspected, but a skiagram of the chest showed no lung infiltration. Under the instructions of his office doctor, he sought admission to this hospital for an investigation.

No relevant past illness or family history was available. He was of regular habits. Being an insurance assistant, he frequently had to tour.

Examination

General.—The patient was sparely built and weak; there was no evidence of toxæmia. The temperature on admission was 101°F.

Alimentary system.—The tongue was coated and moist. The appetite was poor and the bowels constipated. The spleen and liver were not palpable.

Circulatory system.—Heart—normal size, sounds clear. Pulse regular, 140 per minute. Blood pressure 110/75 mm. of Hg.

Respiratory system.—Respiration rate, 18 per minute. Chest movements symmetrical. Fremitus, resonance and breath sounds normal. There was a little cough, but the scanty sputum showed nothing of significance. The tonsils were enlarged, and there were a few palpable glands in the neck.

Nervous system.—The patient was depressed. He complained of headache and indefinite pains in the body. There was generalized weakness. The eyes were normal, knee jerks feeble, plantar reflex flexor.

Blood.—Total leucocytes—5,000 per c.mm. Differential count—neutrophils 73 per cent, lymphocytes 18.5 per cent, monocytes 8.5 per cent and eosinophils nil. Erythrocytes—5,150,000 per c.mm. Hæmoglobin (Hellige)—108 per cent (14.8 gms.). No parasites were found on repeated examination. The van den Bergh reaction—negative. Agglutination completely negative with *Bact. typhosus* and *para-typhosus* A and B, but positive with *Br. melitensis* (1 in 3,200) and *Br. abortus* (1 in 6,400). The culture was sterile. The Wassermann reaction was negative.

Urine.—Acid, no albumin, no sugar; urobilin was present in excess. The centrifuged deposit consisted of amorphous and triple phosphates and a few leucocytes. The midstream urine was sterile on culture.

Stools.—*E. histolytica* cysts were found only once out of four examinations. No ova was found. *Bact. melitensis* was isolated in culture.

Diagnosis

When the results of the various examinations were obtained, the case was diagnosed as undulant fever, the diagnosis being based on the agglutination reactions, and on the clinical picture—bouts of irregular fever, sweating and pains in the body. The spleen was however not palpably enlarged. Further investigations consisted of special blood culture for *Brucella* organisms, and repeated agglutination tests. The culture was negative but there was a rise in agglutination titre (see figure 1).

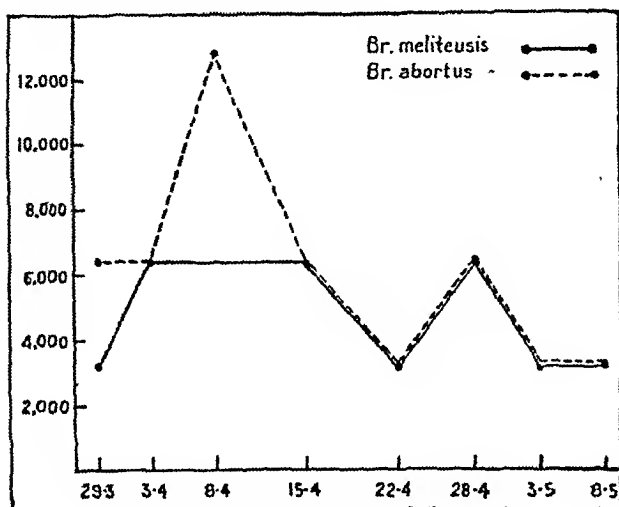


Fig. 1.—Showing agglutination titre.

Treatment

For a week after admission while various investigations were being carried on, the patient was given an alkaline mixture four hourly and palliative treatment with analgesics and sedatives. During this period, he had an irregular remittent fever (see figure 2) and pains in the muscles and joints. He was constipated. He sweated profusely at times.

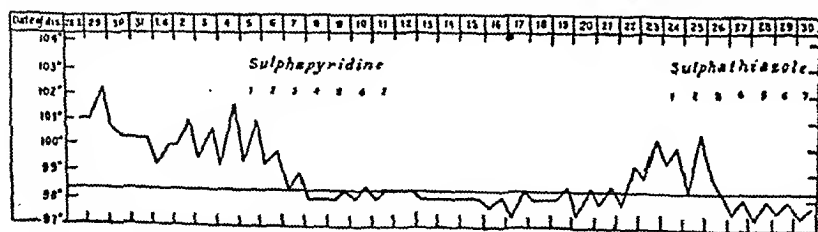


Fig. 2.—Temperature chart showing the apparent result of sulphapyridine and sulphathiazole in controlling the fever.

On 5th April he was put on sulphapyridine—one tablet (0.5 gramme) four hourly. The temperature was normal by the fourth day. The drug was given for seven days altogether, and then he was given a 'tonic' mixture and full diet.

On the 21st he did not feel well, and he had a temperature of 99°F. This was attributed to excessive walking. Next day, however, it rose

up to 100°F. and higher on the following day. On the 24th he was put on sulphathiazole—one tablet (0.5 gramme) four hourly, and the temperature was normal on the third day of its administration. It was however continued for another four days. He had no more fever while in the hospital. He felt better, and his general condition steadily improved, but he did not put on any weight. He was discharged on 12th May with instructions to report if there was a recurrence of fever.

A fortnight after leaving the hospital he had an attack of fever; he took another course of sulphapyridine which controlled the fever in three days. We heard no more of him.

Summary and discussion

A case of undulant fever, a relatively rare disease in this country, is reviewed. The onset was influenza-like, and the initial febrile course resembled typhoid fever. On admission to the hospital, the features observed were irregular fever, indefinite pains in the muscles and joints, headache, malaise, sweating, loss of weight and tachycardia. The symptoms were on the whole of mild character, and the patient did not look very ill.

The source of infection could not be traced. The agglutination reactions were positive in high dilutions with both *Brucella melitensis* and *Brucella abortus*. This test is considered to be the most reliable of the specific tests, other than the isolation of the causal organisms. There was no significant difference between the titres obtained for the two organisms. Moderate enlargement of the spleen and anaemia is said to be common in this disease, but none was evident in this case.

The patient had two bouts of fever while in the hospital, and was given a course of sulphapyridine during the first, and of sulphathiazole during the second. The temperature was normal about the third day of administration on each occasion, but neither of them prevented the subsequent febrile relapse. Administration of the drug for a prolonged period was considered but was not resorted to, as the total white cell count was only 5,000 per c.mm.

Conclusion

The treatment of undulant fever still remains unsatisfactory. The introduction of sulphonamide preparations raised hopes of a specific, and a number of reports have been published without uniform results.

The case under discussion demonstrates that both sulphapyridine and sulphathiazole had a more or less immediate action in controlling fever, but not the subsequent bout of fever.

Acknowledgment

Our thanks are due to Dr. L. Everard Napier, under whom the patient was admitted, for his kind permission to report this case.

EFFECT OF REDUCTION OF SURFACE TENSION ON MOSQUITO PUPÆ

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In *Rev. Appld. Entom.* (B) XXX, (12) 188 (1942) there is an abstract of Manzelli's work on the above subject, taken from *Proc. N.J. Mosq. Extn. Ass.* for 1940. This author found that treatment with concentrations of actual soap as low as 1 to 1,000 caused death through reduction of surface tension, and suggests that the method is useful for dealing with breeding in such places as barrels, where additional dilution cannot occur. The review does not state what species of mosquito Manzelli worked with, but as the method appeared to have possibilities against *stegomyia* in this country, I repeated the work, using a saturated soap solution added in varying proportions.

The results are given in the table below:—

Stegomyia fasciata

Saturated bar soap solution dilutions

CALCUTTA TAP WATER: TEMPORARY HARDNESS 11.50; PERMANENT HARDNESS 1.50

Dilution	Number of specimens	Time to death, minutes
1-50	P.4	45
1-50	L.6	165
1-100	P.7	140
1-300	P.6	180
1-400	P.6	Hatched
1-500	P.6	"
1-500	P.6	"
1-800	P.6	"
1-1,000	P.7	"

DOUBLE-DISTILLED WATER

Dilution	Number of specimens	Time to death, minutes
1-500	P.2	135
1-500	P.6	105
1-600	P.9	100
1-750	P.9	Hatched
1-1,000	P.8	"

P = pupæ. L = larvæ.

Even with double distilled water, no result was found in dilutions greater than 1 to 600, and with Calcutta tap water no result at over 1 to 300. At this dilution, pupæ of *C. fatigans* died, but after much longer intervals. The effect seems to occur during emergence. In very strong solutions, larvæ are seen to be affected.

With the very hard water of the average Calcutta area tube-well, the soap is thrown out of solution at once, and with such waters the method is inapplicable.

HÆMOLYTIC ANÆMIA

By P. N. CHUTTANI, M.D. (Punjab), D.T.M. (Cal.)

CASES of hæmolytic anæmia, other than of malarial origin, evoke considerable clinical interest. Two such cases are here recorded; the first seemed to arise in association with ulcerative colitis and the second was possibly a case of congenital acholuric jaundice.

Case 1.—Mahmud Ali, male, aged 23 years, was admitted on 27th July, 1939, into the Mayo Hospital, Lahore, with complaints of diarrhœa, extreme weakness, palpitation and breathlessness. Diarrhœa was of three years' duration but the other complaints were of one year's duration.

History.—No relevant past illness or family history was available. There was no evidence of dietetic deficiency. The present illness started suddenly three years before, onset being with diarrhœa and later the appearance of blood and mucus in the stools. Ten to fifteen stools a day were sometimes passed. This continued irregularly for about a year, when tenesmus and passage of blood ceased, but the patient continued to pass mucus and loose stools, but fewer in number. He had no fever. He gradually grew weaker and at the time of examination could not walk unassisted. Immediately before admission he had been passing only 2 to 3 stools a day, occasionally with mucus.

Examination.—The patient was a very thin and obviously anæmic individual; the skin was lemon yellow; the mucous membrane of the mouth showed anæmia and icterus; the conjunctivæ were moderately icteric. The descending colon occasionally showed peristalsis visible through the thin abdominal wall. Splashing could be elicited in the right iliac fossa, and the whole colonic area was tender. The spleen was just palpable on deep inspiration. The liver was not palpable.

Laboratory examination.—For hæmatological investigations before and during treatment see the table and figure 1.

The sternal marrow differential count was as follows:—

Polymorphonuclears	..	Neutrophils	7.0
		Eosinophils	nil
		Basophils	nil
Metamyelocytes (including the band-forms).	..	Neutrophils	20.0
		Eosinophils	1.0
		Basophils	nil
Myelocytes	..	Neutrophils	12.0
		Eosinophils	1.0
		Basophils	nil
Premyelocytes	nil
Myeloblasts	nil
Lymphocytes	17.0
Mononuclears	nil
Normoblasts	23.0
Erythroblasts	9.0
Megaloblasts	10.0

For Price-Jones' curve see figure 2. Stools were liquid and green with abundant mucus but no blood. Microscopically 7-8 pus cells and occasional red blood cell were seen per 1/6th field. No protozoal or helminthic infection was detected. The urine showed marked excess of urobilin. The Wassermann reaction was negative. There was achlorhydria after oatmeal, but histamine injection produced free acid secretion. The report on sigmoidoscopic examination was 'Sigmoid acutely inflamed, red, congested and like pile of velvet all along. Mucus and faecal matter keeps on trickling from above all the time'. The transverse folds were not visible and the whole field was regarded as consisting of granulation tissue.

Treatment.—Details of the liver and iron therapy used are shown in figure 1. Dilute hydrochloric acid was also given (drachm doses).

For the bowel condition the patient was given ordinary doses of saline for the first three days, and later bismuth and chalk mixture; after three

Iron (*Ferri et ammon cit.* 90 grs. daily).
Liver injections (*Campolon* 42 c.cm.: *Lilly* 6 c.cm.).

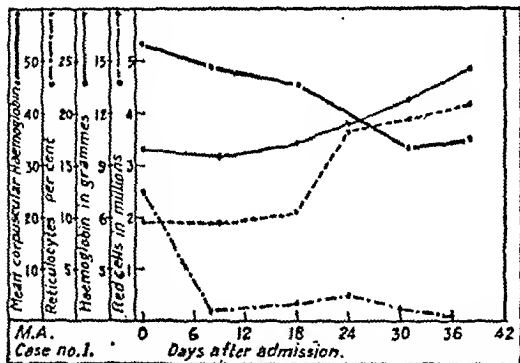


Fig. 1.—Hæmatological details of case 1 before and during treatment.

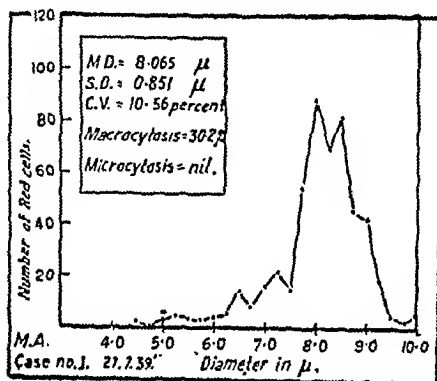


Fig. 2.—Price-Jones' curve of case 1.

weeks $1\frac{1}{2}$ per cent tannic acid retention enemas (6 oz. bi-weekly) were given.

Progress.—Within two weeks of beginning of the treatment, the patient was passing only one stool a day and felt much better. Jaundice had almost disappeared—only a faint tinge was present at this time. A month after admission, even this sub-icteric tinge was completely absent, the van den Bergh reaction was negative, and the total red cell count had doubled.

Discussion.—It is quite definite from the evidence provided, namely, a moderately severe hæmolytic jaundice (positive indirect van den Bergh and acholuria), reticulocytosis (12 per cent) and marked urobilinuria, that there was marked hæmolysis going on in the patient before the treatment commenced. What was the cause of this hæmolysis? Was it due directly to the condition of the colon (and the hæmolysins (?) generated) or was it consequent upon the anæmia with its 'defective products of hæmopoiesis' the red cells being destroyed by a 'relatively normal reticulo-endothelial system'. The latter explanation has been suggested to account for hyper-bilirubinæmia in Addisonian anæmia (Napier, 1939; Davidson and Fullerton, 1938) as opposed to the pigment non-utilization hypothesis propagated by Witts (1932). But in this case the degree of anisocytosis was not marked and the intensity of hyper-bilirubinæmia far exceeded that in Addisonian anæmia. In addition there was the degree of reticulocytosis which is absent in untreated and unremitted Addisonian anæmia: in fact the latter condition is not now regarded as a true hæmolytic anæmia. These points go against any such

TABLE

	Date	Hæmoglobin in grammes	Red cells in millions per c.mm.	Mean corpuscular hæmoglobin.	Mean corpuscular diameter.	White cells in thousands per c.mm.	Neutrophils per cent.	Lymphocytes per cent	Eosinophils per cent	Mononuclears per cent	Normoblasts	Punctate basophilia, or polychromatophilia	Indirect van den Bergh	Reticulocytes in per cent of red cells
Case no. 1	27-7-39	10.089	1.940	53.10	8.065	4,375	50	50	nil	nil	+	+	++	12.0
	4-8-39	9.405	1.930	49.50	..	3,125	26	73	1	nil	+	—	++	1.0
	13-8-39	9.747	2.190	46.41	..	3,000	58	41	1	nil	..	—	..	1.5
	21-8-39	..	3.750	7,500	72	26	nil	2	—	—	..	2.0
	28-8-39	12.825	3.840	33.75	..	5,000	48	50	nil	2	—	—	..	1.0
	5-9-39	14.193	4.140	34.61	..	6,250	58	41	nil	1	—	—	..	0.25
Case no. 2	30-11-38	..	2.40	..	7.576	8,750	52	43	5	nil	+	++	+	8.0
	28-12-38	..	2.57	8,125	65	33	1	1	18.0, on 10-12-39.
	6-1-39	..	2.88	5,825	50	50	nil	nil	27.0 " 20-12-39.
	13-1-39	..	2.50	6,250	45	55	nil	nil	22.0 " 31-12-39.
														24.0 " 6-1-39.
														20.5 " 13-1-39.

Mean corpuscular average thickness on 30-11-38 = 2.12μ .

simple explanation for the degree of hyperbilirubinæmia seen in this individual. But there is the striking fact that all evidence of excessive hæmolysis, including the hyper-bilirubinæmia, disappeared completely when liver therapy (presumably) produced prompt improvement in the blood picture; this fact lends support to the suggestion that anæmia did play some part in the hæmolytic process that was going on. The possibility that the cessation of hæmolysis was spontaneous and not a result of treatment, is considered too remote to merit serious consideration.

Regarding the bowel condition there arise three questions: (1) Did it have any direct relationship to the hæmolysis exhibited by the patient? (2) Was it responsible for the production of anæmia? and, lastly (3) What was the ætiology of the bowel condition itself?

That the bowel condition was not the sole cause of hæmolysis is perhaps clear, because otherwise it is impossible to explain the disappearance of the hæmolysis after liver therapy had improved the blood picture. As has been mentioned above, the anæmia, by itself also could not account for the hæmolysis. The usual method of explaining similar problems by assigning part of the blame to each of the factors is, perhaps, the best to adopt in the circumstances. The history of the present illness, with no previous history of defective diet, leads to the presumption that the ball was set rolling by the bowel condition. The latter with its diarrhœa, produced a deficiency of factor present in liver and in marmite and this happens not infrequently in chronic bacillary dysentery and allied chronic bowel diseases (Strauss, 1934; Keefer *et al.*, 1931; Witts, 1932a). A macrocytic hyperchromic anæmia which brought in its wake a hæmolytic process (aided perhaps by the 'toxæmia' or the hypothetical hæmolysins produced by the original bowel condition) was the next phase. The original bowel condition, which presumably grew worse as the anæmia advanced, and the hæmolytic macrocytic hyperchromic anæmia thus set up a regular vicious circle and both the anæmia and the bowel lesions of the bowel increased. At the time of examination, this vicious circle was in full play, but the liver therapy broke one link by curing the anæmia, and the hæmolysis stopped suddenly and the bowel condition also improved.

The presence of an infective agent in typical hæmolytic anæmia has been rarely demonstrated, but a few instances are on record. For example, Davidson and Fullerton (1938) record a case of hæmolytic anæmia in which they discovered *Salmonella-Dublin* infection though the ætiological association of the latter is not clear.

It would not be irrelevant here to refer to the experimental work of Dameshek and Schwartz (1938) on which is based the modern tentative conception of hæmolytic anæmia, that is, of their causation by definite hæmolysins. Even the congenital acholuric jaundice 'seems likely to

fall into this class, necessitating perhaps the abandonment of Haden's theory' (Whitby, 1939). However, the types of hæmolytic anæmia, namely, the acute hæmolytic anæmia of Lederer, the paroxysmal hæmoglobinurias, the acquired type of hæmolytic jaundice, and even congenital hæmolytic jaundice, which are quoted by the above authors as being probably caused by hæmolysins, do not respond to liver therapy, as did the present case.

What was the bowel condition? Chronic bacillary dysentery, and chronic ulcerative colitis, were the two possibilities. The sigmoidoscopic appearances of all stages of chronic ulcerative colitis described by Chopra and Ray (1939) in their series of 120 cases did not cover this particular patient. The latter authors do not support the idea of any relationship between chronic bacillary dysentery and chronic ulcerative colitis, but Hurst (1937) believes that '... ulcerative colitis is a form of bacillary dysentery'.

Case 2.—Niaz Ali, male, aged 15 years, was admitted on 30th November, 1938, into the Mayo Hospital, Lahore, with complaints of breathlessness, palpitation, low fever and lack of increase in weight. The duration of his complaints was about five years.

History.—Family and personal histories yielded nothing relevant. No member of the family had suffered from anæmia or jaundice. The patient had never felt fit but had not ever been ill enough to be absent from school. He had been conscious of his complaints for about five years previous to admission but his parents stated that he had had an enlarged spleen and an anæmic appearance since the age of three. When the blood was examined at the Mayo Hospital, Lahore, the parents were told he was suffering from anæmia.

Examination.—He was a very thin boy with a pale lemon yellow skin. The conjunctivæ bore an icteric tinge. The spleen was enlarged four fingers below the costal margin, was hard and extended medially to the umbilicus. The liver was also enlarged about three fingers below the costal margin and was hard. There was no ascites.

Laboratory examination.—For hæmatological investigations see the table and figure 3. The Price-Jones'

Iron (Ferri et ammon cit. 90 grs. daily).
Liver injections (Campolon 70 c.cm.).

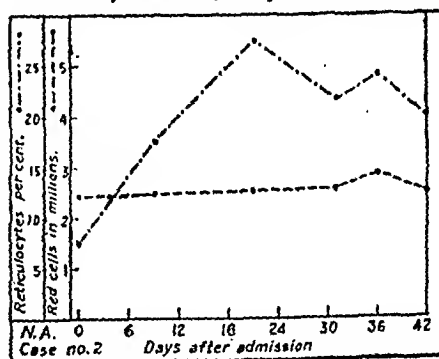


Fig. 3.—Hæmatological details of case 2 before and during treatment.

curve is shown in figure 4. Sternal marrow showed a normoblastic reaction (normoblasts 60 per cent). The ordinary fragility test (quantitative test not done)

*The hæmoglobin estimations having been carried out by Tallqvist scale are not reported.

revealed no abnormality. The urine showed excessive amounts of urobilin and traces of albumin. No bile pigments or salts were present. The stools showed no helminthic or protozoal infection. The Wassermann

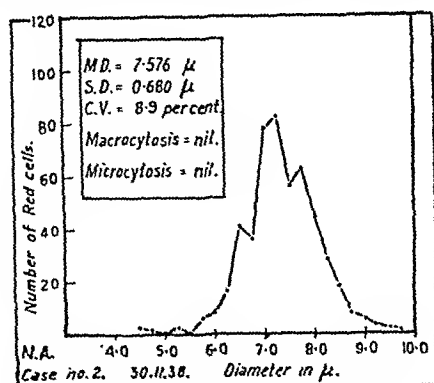


Fig. 4.—Price-Jones' curve of case 2.

reaction was negative. Gastric analysis showed no abnormality. Radiological examination of the skeleton showed nothing abnormal. The gall-bladder was not examined for stones.

Treatment.—Although the patient had already had an extensive course of iron and liver treatment before admission, these were tried again. Four c.cm. of campolon were injected twice weekly and a total amount of seventy c.cm. was thus administered. No improvement resulted either in the blood picture or in the clinical features. Splenectomy was advised but was refused.

Discussion.—The patient showed no increased fragility of the red cells in the crude test performed, but this may have been on account of the anaemia (Creed, 1938). There was no spherocytosis: this is corroborative of the absence of increased fragility. The history, the clinical features and the laboratory findings of a chronic haemolytic anaemia, suggested acholuric jaundice (Chauffard and Minkowsky type) but in the absence of positive haematological support (i.e. spherocytosis and increased fragility) it is

difficult to be dogmatic on this point. Normal fragility of red cells, however, is not incompatible with a diagnosis of acholuric jaundice: about 10 per cent of the patients fail to exhibit any excessive fragility (Whitby and Britton, 1942).

Summary.—Two cases of haemolytic anaemia are reported, and their diagnosis is discussed. A brief allusion is made to modern experimental work throwing light on the probable pathogenesis of the haemolytic states.

Acknowledgments.—I wish to thank Lieut.-Colonel A. Chand, I.M.S., late Professor of Medicine at Lahore, for his permission to publish the records of his patients investigated by the author. Thanks are also due to doctors D. C. Gupta and P. N. Luthra, my old colleagues, for the unstinted help so willingly afforded.

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A Mirror of Hospital Practice

TORTICOLLIS AND CONVULSIONS APPARENTLY DUE TO ASCARIASIS

By K. C. GHOSH, L.M.F.

Medical Officer, Red Bank Tea Estate, Daicheng, Jalpaiguri District

ON the 27th December, 1942, a boy aged 8 years, was brought to me. His mother said that he suddenly awoke in the previous night crying with extreme pain on the left side of the neck. He was 'nearly dying' and his body was convulsed when the pain increased in intensity.

On examination.—He had typical wry neck, the face being turned to the right side and the left sterno-mastoid being in a state of tonic contraction. He was conscious but could hardly open his mouth with consequent impairment of speech. There was no rise of temperature. Nothing abnormal was found in the heart. Pupils were equal. No injury or ulcer was

noted. Reflexes were not elicited. He had had no such attack before. During examination the boy suddenly shrieked, due to aggravation of pain, and had a convulsive seizure of very short duration with a tendency to opisthotonos. This had happened twice or thrice at night.

Treatment: 1st day.—The boy was kept at absolute rest and given A.P.C. powders and calomel at night followed by magnesium sulphate in the morning.

2nd day.—His condition was found to be the same. A salicylate mixture with bromide was prescribed. By noon his bowels opened and two round worms were passed. In the evening I found no amelioration of his symptoms, and the patient had spasm again during examination. His heart rate was rather slow. It struck me then that this symptom-complex might be due to irritation by the worms. The mixture was then withheld, and he was given santalin 3 grains with calomel at bed time followed by saturated solution of magnesium sulphate 1 ounce in the morning.

3rd day.—Bowels moved freely, and he passed altogether 18 round worms in 24 hours. He had only one convulsive seizure in the morning while I was auscultating his heart. At night he seemed to be almost cured and slept quietly.

4th day.—He passed four more round worms in the morning, but had no more fits of pain and spasm. Face and neck became normal. He is now quite fit.

For want of facilities his stool could not be examined microscopically for ova, so he was given another course of santonin after 3 weeks, but no more worms were passed.

My thanks are due to Mr. J. C. Bose, manager of this estate, for his kind permission to report this case.

A FEW SUGGESTIONS FOR BLOOD BANK WORKERS

By K. V. NAYAK, M.B., B.S.

Pathologist, K. E. M. Hospital, Secunderabad (Deccan)

THE following few suggestions, though superfluous to many, are offered with the hope that they may be useful to workers in some Blood Banks in India.

Wassermann reaction.—Where the Wassermann reaction is done, the following single tube method is very helpful as it is less time consuming and laborious than the routine test. It consists in carrying out the test with one volume each of 1 in 5 diluted inactivated serum, antigen, 3 M.H.D. complement and sensitized cells. If there is complete hæmolysis, the result is recorded as negative and no further action is taken. In the absence of hæmolysis, the test is repeated with the full set of four tubes. It has been observed that only one or two out of a hundred bloods required complete testing. In this connection it may be of interest to note that in many Blood Banks in England when pooled serum and plasma are banked, neither the Wassermann nor the Kahn test is done, as, in the considered opinion of many workers, these are unnecessary. The temperature of 4°C. at which these products are kept for more than 60 to 80 hours exerts a lethal effect on the *Treponema pallidum*. An additional safeguard is provided by the Seitz filter.

Needle sterilization.—Weintraud's saline needles 18 S.W.G. size with a square mount and adaptor are used in our Blood Bank. The needles and cannulas, fitted with stilettes projecting beyond the points to prevent their damage during manipulation, are arranged neatly in a rectangular copper bath having a lid and a spout at one corner. Liquid paraffin is poured to cover them and the temperature is raised by means of a spirit lamp to 140°C. for a couple of minutes. The lid is put on, and the paraffin poured over into an empty cigarette tin and drained completely. The needles are then ready for use. Any oil sticking inside the lumen is removed by blowing air through with a sterile syringe. Liquid paraffin can be used over and over again, but turns brown and charred after a time and has to be replaced. If a thermometer of 200°C. is not available, a bread crumb thrown into the heated paraffin indicates, when charred,

the requisite temperature. By employing this method, needles do not get rusty, their inner and outer surfaces retain the polish, serum does not get hæmolyzed and a high degree of sterility is obtained. Water sterilization has none of these advantages.

Needle sharpening and care.—With the rising cost of needles and the difficulty of replacement, it is of the utmost importance that they be used with care. If the following procedure is adopted, needles may be made to last a long time and retain their sharpness, thus making blood donation a painless affair. Water is forced several times through the needles and cannulas immediately after use with a syringe. They are then inspected one by one with a hand lens, or preferably examined under the low power of a microscope while fixed on a slide with plasticine. If the points are damaged, fresh ones are made with the help of a sharpening stone. Hard 'Arkansas' is the best. The needle is held firmly between the thumb and the forefinger with its bevelled surface down and the pointed end rubbed against the stone with a to and fro movement along its length. Any rotatory movement is likely to cause facets and must be avoided. Beveling is complete in about a dozen strokes. The angle between the needle and the stone determines its nature—the greater the angle the shorter the bevel and vice versa. Attention is next paid to the point and its cutting edges. Two or three sharp strokes on either side of the bevelled portion with the side of the stone does the job. Triangular cutting edges can be made by a similar treatment to the back of the needle point. All manipulations are controlled by observations under the microscope. It is quite easy to sharpen any bad needle in 10 to 15 minutes. No needle, however bad, must be thrown away until an attempt has been made to mend it. It may sometimes be advisable to cut off the needle point, which must be done with the stilette inserted to prevent blocking of the lumen, and a fresh point is made. The above procedure of sharpening can be successfully applied to any type of needle, from the lumbar puncture needle to the smallest intra-dermal one. Needles must be wiped with a clean piece of muslin and stored dry with the stilettes in place. The use of emery or sand paper for cleaning thins and leaves grooves on the barrel, and must never be resorted to. 'Brasso' and sylvet cloth may occasionally be employed to give a little polish. The Secunderabad Blood Bank has been using one dozen needles from the beginning, over 2,000 donors have been bled and the needles are still as good as new.

Published with the kind permission of Lieut-Colonel J. C. Pyper, I.M.S., Medical Officer, K. E. M. Hospital, Secunderabad (Deccan).

CORRIGENDUM

In the article by Dr. R. Mahadevan in our June number, on page 279, line 28, right hand column 'a 3 to 4 inch incision was made with a diathermy knife' should read 'a $\frac{3}{4}$ inch incision'.

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Indian Medical Gazette

JULY

ADVERTISEMENTS

A MEDICAL journal exists for the purpose of conveying useful information to the medical profession. From the body of the journal the doctor gets useful information of a professional nature, but from the advertisement sections he should be able to get information regarding the medical supplies that are available, their nature, their quality and so on, and this information may be extremely valuable. The publishers of medical journals publish advertisements, not merely because they help to finance the journal, but also because they are of real use to their readers, and moreover because they help the manufacturers and suppliers of good products to make their products known. Good advertisements of good products are an essential part of a good medical journal. It has often been said that the quality of a journal can readily be judged from the quality of its advertisements.

Before the war, a large proportion of our advertising space was taken up by foreign manufacturers and agents whose products had a world-wide reputation. Many good Indian firms also advertised in our pages, and we have always tried to encourage the advertisement and use of good products produced in India.

Now the imports of many foreign medical products have ceased or been much reduced; Indian firms of repute are striving with considerable success to meet the increased demand for reliable medical supplies, and they are naturally advertising their products. All this is good, and as it should be, but there is a less satisfactory aspect of the present situation. The Indian Chemical Manufacturers Association, in a circular referred to in our present issue, draws attention to 'the trade in spurious drugs by bogus and unscrupulous manufacturers'. Such persons are trying to exploit the present shortage of supplies by putting on the market all kinds of spurious remedies for malaria, dysentery and so on, and moreover sometimes try to advertise their products in the medical press. We strongly support the plea of the Indian Chemical Manufacturers Association, that steps be taken to control this evil.

The publishers and the editor of the *Indian Medical Gazette* are keen to prevent their journal being used for the advertisement of spurious medicines, medicines of poor quality, quack medicines, medicines of any kind for which exaggerated claims are made. With this object in view, all advertisements have to be approved by the editor before they can be accepted, and not infrequently advertisements are refused because the product advertised does not appear

to be a scientific one, or because the claims made for it appear to be unwarranted.

Of course it is quite impossible for the editor to make an analysis or a clinical trial of every product advertised in the journal, but not infrequently the advertisements submitted, or the literature put out by the makers, will make this quite unnecessary.

We will quote a few examples of advertisements which have recently been rejected by this journal. Some have been 'infallible cures' of malaria but containing 'no quinine or arsenic'. One remedy was guaranteed 'to cure every case of dysentery' within a few days. One remedy was an arrowroot preparation said to be an excellent food for infants. Others have been 'sovereign remedies' for 'all respiratory diseases' including, one supposes, tuberculosis. One advertisement stated that the product cured most fevers, but if the fever had not subsided after a few weeks' treatment, a doctor should be consulted! Some advertisements have been rejected, not because the remedy appeared to be useless, but because the claims made for it were grossly exaggerated and unscientific.

It has been felt that to allow this journal to be used for such advertisements was wrong, and if we did publish them, our readers would rightly feel insulted. Such advertisements have no place in medical journals of repute.

We think that some manufacturers and agents do not seem to realize what kind of advertisement is likely to appeal to the doctor. A doctor does not want to read general vague statements about a product. He wants brief but detailed information. Regarding mixtures he wants to know what are the ingredients, and in what amount they are present. Of chemical compounds he wants to know their nature, and not merely the proprietary names that the manufacturers choose to give them. Advertisements of newly introduced products that do not give this information always arouse the suspicion of a doctor reading the advertisements.

Sometimes an advertisement, and sometimes the literature put out by a firm or an agent, may contain a list of a dozen ingredients in a preparation, and naturally one wonders how many of them are actually there, and what would be the use if they were. Also the long screeds of pseudo-scientific nonsense, easily detected as such by the critical medical reader, always arouse a suspicion of quackery.

On the whole it will be found that the firms of the highest reputation are the most modest in the tone of their advertisements. From firms of repute, whether Indian, British, or American, advertisements are usually attractive, simple, informative and modest in their claims. Such firms practise what is sometimes called ethical advertising. Actually we think that American medical advertising is much the best. A doctor will read the advertisement section of American journals for information, for pleasure,

and sometimes for amusement. Perhaps this is why American journals usually do not allow advertisements to be 'interleaved' in the text of the journals. They know that this is unnecessary, for the advertisements will be read without the use of this subterfuge.

One type of advertisement which we feel should never be allowed in a medical journal is the interleaved advertisement printed to look like the ordinary text matter of the journal, so that the reader is deceived into reading it. To his annoyance, when he gets to the end, he finds that it is an advertisement. This is bad advertising, for a firm to annoy a possible client. By an accident, one such advertisement (and of a well-known firm of high standing) got into our pages recently; our refusal to continue this type of advertising caused misunderstanding and the cancellation of the contract. To maintain reasonable standards, such sacrifices have to be made.

We therefore appeal to our advertisers, and prospective advertisers if they have medical supplies of good quality, to give us good, simple, straightforward, informative, and attractive advertisements. By such methods will the medical industries of India benefit.

To our readers we wish to say that we shall try to maintain a high standard in our text matter and in our advertisements, and to see that our pages are not used for giving publicity to quack medicines, or to exaggerated claims for any kind of medical supplies.

FIRST-AID POSTS

On page 361 we reprint from an English journal an editorial note on this subject. It seems to be the general opinion based on experience that for dealing with air-raid casualties, the two essential services are the mobile first-aid party (including doctors, nurses, ambulance, etc.) and the fully equipped hospital. First-aid posts have not been nearly so much used as was expected, and have often proved wasteful in

personnel, equipment, and in precious time. A patient's life may be endangered by the delay caused by taking him to an aid post rather than direct to the hospital. Large numbers of aid posts in England have been closed as redundant.

We have a feeling that in some cities in India, the same situation may possibly be found. We wonder whether the authorities have considered carefully whether all the first-aid posts are worth while. It is quite clear that the inadequately staffed and equipped first-aid post can be a public danger.

'HEMERALOPIA'

On several occasions lately we have seen the word 'hemeralopia' used as a synonym for night blindness. We thought that the meaning was 'day blindness', and we have therefore removed this word from manuscripts as being incorrect.

We have however just read the following phrase in the *Lancet*: 'night blindness better referred to for psychological reasons as hemeralopia'.

We have therefore looked into the matter closely, and have consulted medical dictionaries. The two medical dictionaries consulted are both good ones and both American.

Dorland's is not at all helpful. He gives two meanings for hemeralopia, the first being 'day blindness' (i.e. poor vision in bright light) and the second, 'night blindness, or nyctalopia'. Stedman's is much more helpful. He gives one meaning only, 'day blindness', but also states 'often incorrectly used to denote night blindness or nyctalopia'.

The derivation of the word is quite clear, (hemera = day, alaos = obscure, and ops = eye, hemeralopia = weak vision by day).

In the word nyctalopia, the Greek root nykt (= night) is substituted, and the word therefore means weak vision by night.

We propose therefore in this journal to use these words in the sense indicated by Stedman, which seems obviously correct.

Special Article

THE ANTERIOR SHOULDER IN PREGNANCY AND LABOUR: ITS PRACTICAL UTILITY

By N. A. PURANDARE
Bombay

To locate the anterior shoulder during palpation of the abdomen of a pregnant woman in the later months is of great help in ascertaining what is the exact position of the foetus, how far the head has descended into the pelvic cavity, or whether it has entered the brim at all or is lying free above it. Moreover, during labour, the determination at intervals of the site of the

anterior shoulder will enable the examiner to know whether the head is making progress, and also whether it is undergoing internal rotation after it has reached the pelvic floor. The position of the anterior shoulder may tell us whether the head has actually descended to the vulval outlet, or whether that part of the head which is visible at the vulva is in reality merely a swollen caput succedaneum. Thus it can be readily perceived that the determination of the site of the anterior shoulder is not merely of academic interest but of practical importance. Now the first question that naturally arises is, why is the anterior shoulder, such a small

part, chosen for study, and why is so much significance attached to it? There are other means of distinguishing between the anterior and the posterior positions of the vertex presentation, such as determining the direction of the groove between the head and the trunk at the situation of the neck; locating the back of the child and finding the site where the foetal heart sounds are best heard.

As to the groove, it is more serviceable when the occiput is directed forwards, i.e., in the anterior positions. It is then found running obliquely from the chin down to the occiput. In the first position, it can be traced from the right side down to the left; while in the second position, it begins above on the left side and comes down to the right. In this way in the anterior positions, the direction of the groove helps to diagnose the first from the second position. But in the posterior positions the groove is horizontal. It is therefore impossible to distinguish the third from the fourth position by the help of the groove. The groove is therefore of use in diagnosis of the anterior positions only. But it is in the posterior positions that difficulties are more common, and here the groove does not help us.

The back of the child does present a large area, the feeling of which should supply readily the necessary information, and if the back were always forwards and palpable, it would be a very useful guide. But it has been realized that the head more often enters the transverse diameter of the brim, and a result is that the back is more often at the side than forwards. Even in normal anterior positions, the back may not be palpable, and in posterior positions it is of course not palpable.

As to the foetal heart sounds, they are louder in an anterior position and fainter in a posterior one. In this way one has to rely upon one's capacity to distinguish between degrees of intensity. It must be admitted that the sites where the heart sounds are best heard differ in anterior and posterior positions. They are heard well towards the middle in the anterior positions while in the posterior they are best heard towards the flanks.

In view of these difficulties, the position of the anterior shoulder should prove more useful in recognizing not only the anterior from the posterior positions, but also in differentiating between the face positions.

Now we can consider how to locate the anterior shoulder (figure 1). Before proceeding to feel for the anterior shoulder, it is essential to carry out the usual preliminary examination of the pregnant woman. After ascertaining the size of the head palpable above the brim, the situation of the occiput, and direction of the groove, the anterior shoulder is felt for. It is felt as a hard, small, conical part difficult to displace. This immovability of the shoulder should always be borne in mind, because sometimes the fist may form a palpable lump which is likely to be confused with the anterior shoulder. The fist however can be readily displaced.

Should there be any difficulty in discovering the anterior shoulder, it is made more prominent and easily palpable by pressing down upon the buttocks at the fundus, or it can be reached by following along the back, when the fingers will come upon the anterior shoulder.

It must never be forgotten that in both the first and fourth positions, when the back is directed to the left side, the anterior shoulder

is felt on the left side, whereas in the second and the third positions, it is on the right side (figure 2). The height of the anterior shoulder above the pubis indicates how far the head has entered the pelvic cavity, while its distance from the middle line helps to distinguish the anterior from the posterior positions. To take these measurements, the exact site of the anterior shoulder must first be ascertained. Then a line from this point is drawn down to the middle line. The distance from this point of meeting to the top of the pubis is measured, and this gives the height of the anterior shoulder. At the same time the distance from the mid-line to the anterior shoulder is measured.

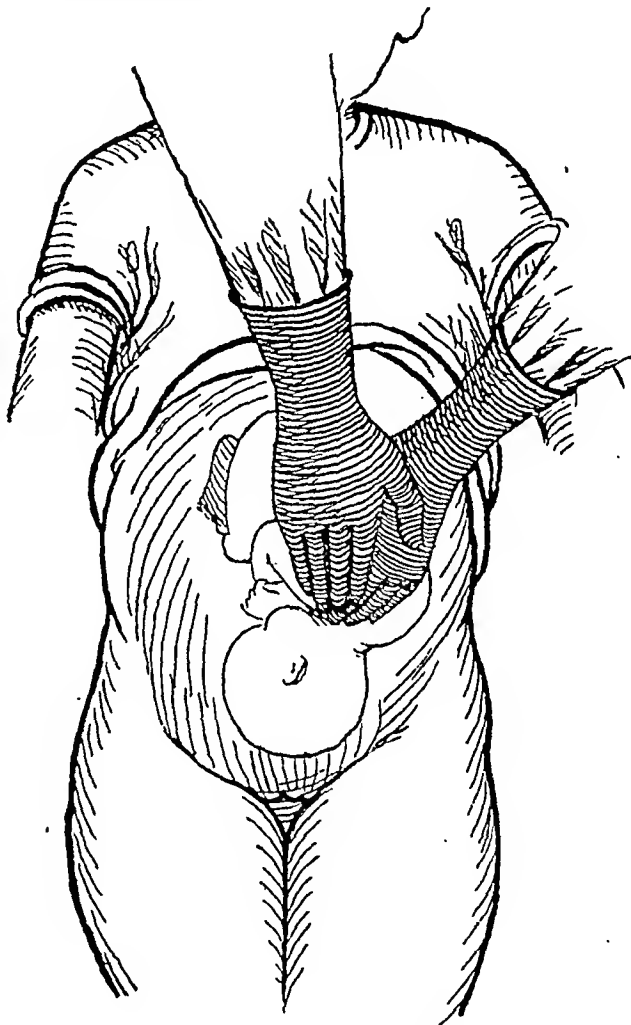


Fig. 1.—The method of palpation of the anterior shoulder.

When the height is 2 inches from the pubis it may be taken that the head is engaged; then nearly three-fourths of the head is down in the cavity, only one-fourth being palpable above the brim. In normal conditions, when the pelvis is of normal dimensions, the average head is smaller than the cavity, and therefore a distinct space is felt between the pelvis and the anterior surface of the head. In the cavity it has gained the ischial spines, lying just at the mouth of the soft birth-canal. The greatest circumference of the head has descended past the pelvic brim. Under these circumstances, when labour begins, the head having already traversed the bony passage, has merely to journey through the lower soft canal. The work that

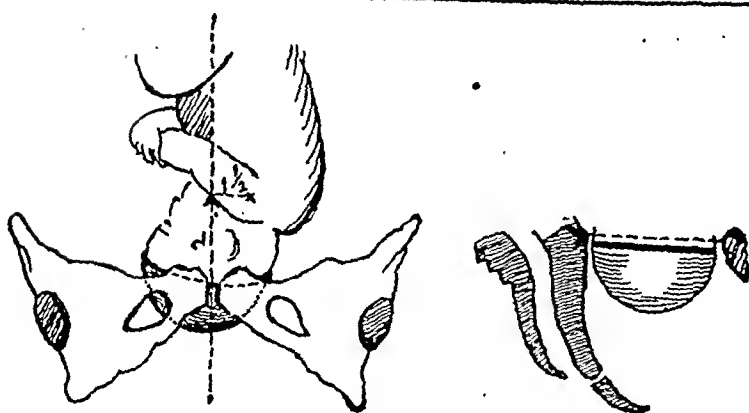
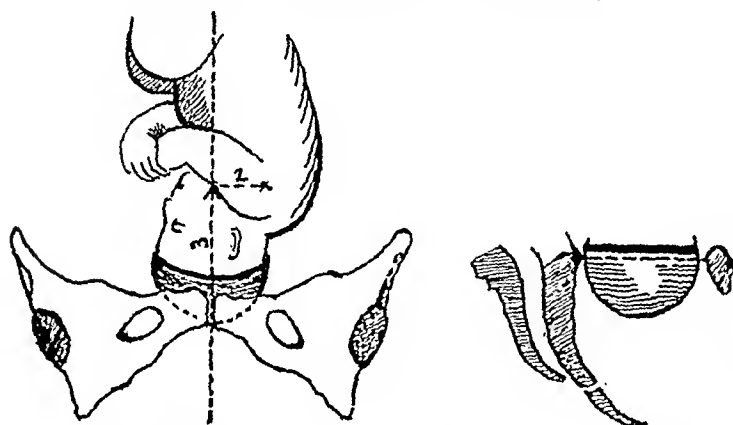
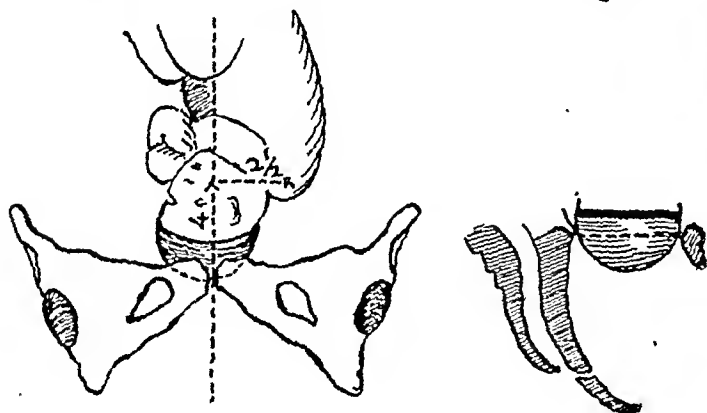


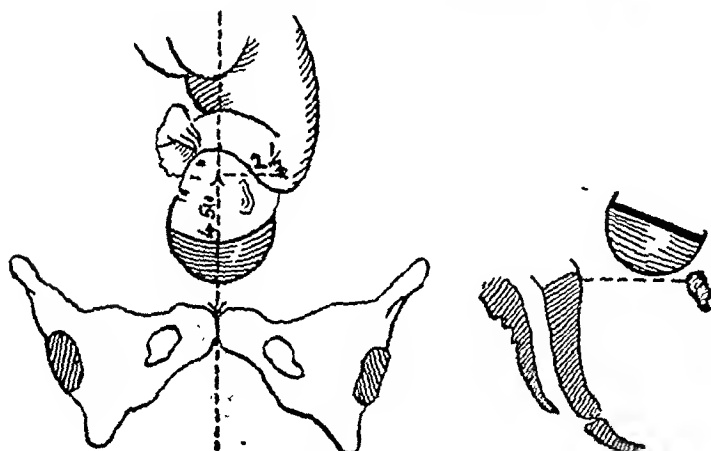
Fig. 2.
Head engaged—anterior shoulder 2 inches high.



Head half engaged—anterior shoulder 3 inches high.



Head engaging—anterior shoulder 4 inches high.



Head floating—anterior shoulder 5 inches high.

the uterus has to do during delivery is relatively little, as it has to propel the head only through this soft muscular canal, entailing less expenditure of energy.

When the distance is 3 inches, the head is half engaged, and half of it is palpable above the brim; it has reached the mid-plane of the pubis; its greatest circumference is at the brim, and therefore it may be in touch with the back of the pubis. As labour sets in, the head has to travel through that part of the bony canal which is below the mid-plane, and then to enter the soft birth-canal. More work than above is thrown upon the uterus, and in consequence the organ has to exert more effort to effect delivery, thus calling for more energy.

When the height is 4 inches, the head has but entered the brim; one-fourth of it is in the pelvis and the remaining three-fourths above the brim; the greatest circumference of the head is naturally above it. When labour begins, the head has to go down through almost the whole of the bony passage before it reaches the entrance of the soft canal. Much more work has to be done than in the above two conditions, and in doing this work, the uterus gets exhausted towards the end, and artificial aid may be then needed to bring about delivery. So long as the organ possesses strength, and the reserve capacity is enough to cope with the work, it may by itself succeed in expelling the child. In a woman who has had a number of previous pregnancies, the wall of the uterus may have been rendered weak, and in later pregnancies it may not contract so powerfully as in earlier ones, and may manifest inertia when the head has descended into the pelvis, and sometimes even after it has approached the outlet.

When the anterior shoulder is at a height of $4\frac{1}{2}$ inches or more, the head is above the brim, and it is floating. It can be moved readily from side to side. This is a serious condition, and needs careful consideration. The head remains floating either because an adequate force is not acting and pressing the head down in the brim, or because the passage is small. The first factor is most commonly seen in the multipara. The second factor is most commonly seen in a primipara. To ascertain which of the two causes is acting, careful examination of the patient is imperative.

The head should be pushed towards the brim to find out whether the former can be made to enter the latter. In a multipara with the history of previous normal easy labours, the head can be made to engage in the brim; whereas in the case of contracted pelvis, it would not be possible to push the head down.

From the above measurements of the height of the anterior shoulder, we can draw conclusions about the engagement of the head. These measurements and the inferences drawn from them are the result of observations made on every case as a routine for several years.

From the distance of the anterior shoulder from the mid-line we can tell whether the position is anterior or posterior.

When the anterior shoulder is from $1\frac{1}{2}$ inches to $2\frac{1}{2}$ inches from the sub-umbilical line, the position is anterior; whereas when it is 3 inches or over, it is a posterior position. When the head is well flexed, the anterior shoulder lies within $2\frac{1}{2}$ inches; but when it is between $2\frac{1}{2}$ inches and 3 inches, the flexion of the head is defective, and the groove at the neck is felt less definitely oblique than usual. When the anterior shoulder is situated at a distance of 3 inches or more, the neck groove is transverse, indicating a posterior position. In the posterior position, this distance from the mid-line varies from 3 inches to $4\frac{1}{2}$ inches.

During labour, as the head descends on the pelvic floor and the internal rotation begins, the distance grows less and less as the occiput comes nearer to the public arch to escape from underneath it. If the distance, instead of decreasing, begins getting greater, it at once suggests, that the normal internal rotation is not occurring, which may happen in a posterior position, and that the occiput is turning backwards toward the hollow of the sacrum. In this way, to measure the distance

of the anterior shoulder from the mid-line is of practical utility as it helps one to determine the position and to know whether in labour the head is undergoing the normal internal rotation or not.

Difficulties and errors in recognizing the anterior shoulder.—Under certain conditions difficulties arise in recognizing the anterior shoulder. If the patient is obese, having a very thick pad of fat in the abdominal wall, it is sometimes very difficult to feel the anterior shoulder. If so, pressure on the buttocks at the fundus forces the anterior shoulder down and

rigid, as is often found in a primipara. A distended bladder may also interfere with the feeling of the anterior shoulder. Should a fibroid be connected with the uterus, especially with the anterior wall, it may create difficulty in locating the anterior shoulder. In labour, during contractions, when the uterus becomes hard, it is difficult to ascertain the position of the anterior shoulder as long as the contraction lasts.

Sometimes some other part of the child may be mistaken for the shoulder. The fist has already been mentioned, but its mobility contrasts with the fixity of the shoulder. Moreover when the presentation is a complete breech with the back behind, the feet are palpable and the heel of either foot is apt to be mistaken for the anterior shoulder. If both shoulders are felt, they are situated wide apart; the anterior shoulder is always at a lower level and palpable immediately above the head. But in spite of these difficulties, the anterior shoulder can usually be readily distinguished.

Some of the advantages derived from taking measurements of the anterior shoulder have been already referred to above.

At the onset of labour, the exact site of the anterior shoulder should be noted, so that it can be followed afterwards. If it is $4\frac{1}{2}$ inches and above, it should at once be apprehended that it is not a favourable situation. If the patient is a multipara, the history of her previous labours should be carefully inquired into, in order to ascertain whether they were all easy or difficult, and if the latter, whether any artificial aid was needed on any occasion. If labours were normal, it must be found out by examination whether the head can be made to enter the pelvis. To do this (figure 4), the patient is placed in the

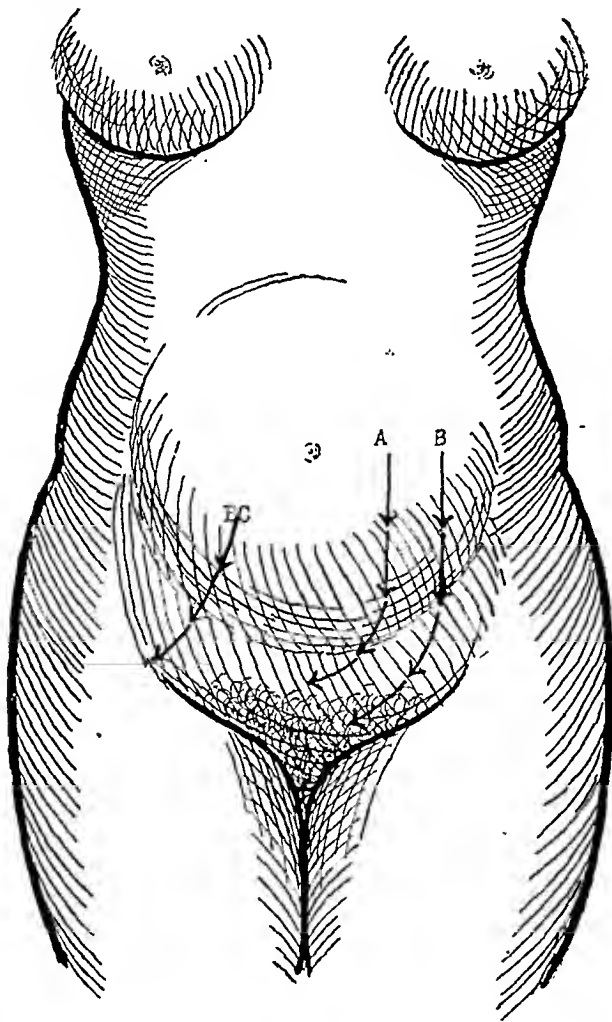


Fig. 3.

- A Progress of the anterior shoulder in anterior position.
- B Progress of the anterior shoulder in posterior position.
- BC Failure of anterior rotation in posterior position.

makes it more prominent, so that it can be felt even through the thick abdominal wall. A difficulty is encountered when there is hydramnios, the great amount of liquor amnii around the child rendering it almost impossible to palpate the different parts of the foetus. Further if during palpation, the patient holds the abdominal wall rigid and tense, the feeling of the anterior shoulder is rendered difficult. The same thing happens when the uterine wall is

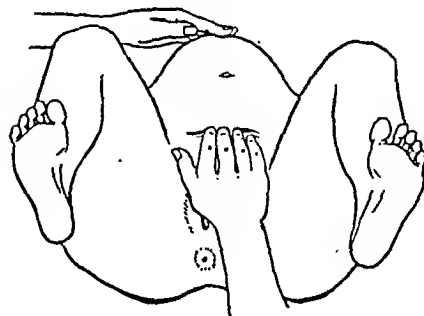


Fig. 4.

The dorsal position in labour.

dorsal position, and the four fingers of the right hand are dipped in above the top of the symphysis pubis. The thighs are then bent over the abdomen and separated, when, in a multipara with normal pelvis, the head will be felt descended into the cavity. Should the patient be a primipara and the head be floating, the situation is grave. In this case, the presence of some cause preventing the head from being engaged is indicated, since the head has normally entered the pelvis long before labour has begun. With regular ante-natal supervision, the cause should

be recognized early, and, if it is a cephalopelvic disproportion, the case might have been set aside for test labour in which the following of the anterior shoulder often proves of great help. If the head descends at an early stage, and the height of the anterior shoulder from the top of the pubis, and the distance from the middle line progressively get less, it can be taken that labour is progressing favourably. For proper judgment, the measurements have to be taken at intervals of half an hour, the heart sounds also being auscultated.

If measurements remain the same, though several hours have elapsed, delivery may have to be aided in the interest of the mother and child. The behaviour of the anterior shoulder will help in making possible this decision relatively early.

The measurement of the distance from the mid-line is particularly useful in a posterior position. Should it decrease and should the anterior shoulder be felt approaching the central line, it will signify that the internal rotation of the head in the birth-canal is proceeding. If however it increases from 3 inches to 4 inches or more, it at once indicates that the occiput instead of turning forwards, is turning backwards towards the hollow of the sacrum.

The measurements of the anterior shoulder are also useful whenever the necessity of applying the forceps occurs. This instrument is not to be used when the height of the shoulder is 4 inches or more. If the forceps be applied in this condition, the head would be subjected to so much compression during extraction that the child will probably be born dead; and the mother will be lacerated. When the height is 3 inches, forceps may, if absolutely necessary, be applied, but the situation is not very favourable to mother or child. As long as the height is 3 inches, it is wise to avoid applying forceps.

When the height of the anterior shoulder becomes less than 3 inches, the situation becomes more favourable, and with the height of 1 inch, forceps delivery is usually easy.

In the case of transverse arrest, the height of the anterior shoulder remains between 3 inches and 2½ inches. When the progress thus appears to be checked, artificial aid is called for and should be given early.

If the occiput rotates backwards, the distance of the anterior shoulder from the middle line increases, but the height of the anterior shoulder goes on decreasing. Should the progress be arrested, appropriate steps should be taken.

Another advantage that is derived from locating the anterior shoulder is that of knowing the exact site where the fetal heart should be listened to. These sites vary according to the height of the anterior shoulder.

In the anterior position, the heart sounds are heard best on a line 2 inches from the middle line, while in the posterior positions on a line 3½ inches to 4 inches from it, and on the side where the back is.

In each of the anterior positions, when the anterior shoulder is 2 inches high, the heart sounds are heard on the lateral line about its middle, or at the height of 4 inches; when it is 3 inches, the heart sounds are

heard on the line at about 6 inches; when the anterior shoulder is 4 inches high, the site of the sound is at about 6½ inches to 7 inches; when the shoulder is at 4½ inches or above, the fetal heart sounds are heard

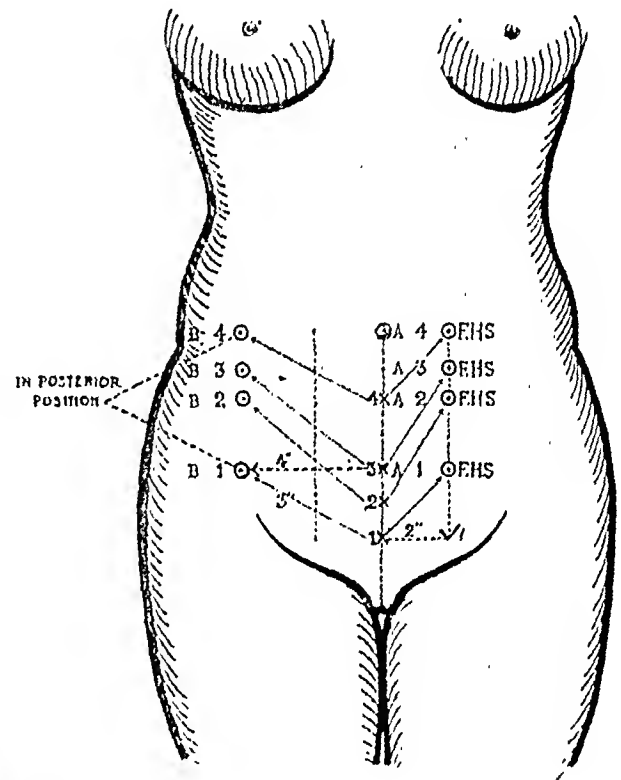


Fig. 5.

- A Indicates anterior position.
- B Indicates posterior position.
- X Indicates height of the anterior shoulder.
- O Indicates fetal heart sounds.

at the level of the umbilicus on the side where the back is lying (figure 5).

In each of the posterior positions, the heart sounds are heard on the side where the shoulder is located, nearly at the same height as in the anterior positions, but in the flanks about 4 inches from the mid-line.

This knowledge may save valuable time in the location of heart sounds.

In general, the determination of the position of the anterior shoulder before and during labour is of great value to the obstetrician.

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Medical News

INDIAN CHEMICAL MANUFACTURERS' ASSOCIATION

THE Committee of the Indian Chemical Manufacturers' Association have issued a circular to the member-bodies in course of which they point out that while they are trying to improve the standard of drugs and medicines, the trade in spurious drugs by bogus and unscrupulous manufacturers has been going on without any check from many quarters. Although the attention of Government was repeatedly drawn to this menace, the enforcement of the Indian Drugs Act of 1940 is still being delayed. The Committee point out that the unwary public are easily deceived by the low prices, labels and clever packings of these faked medicines, particularly quinine and emetine preparations which are considered essential remedies for malaria and other allied diseases.

As this malpractice constitutes a serious menace not only to the Drug Trade but also to public health, the Committee urge both the public and the recognized manufacturers of drugs to co-operate in combating this evil, the former by refusing to buy these spurious preparations at ridiculously low prices and the latter by keeping a strict vigilance on the channels through which these drugs flood the market.

THE INDIAN HONOURS LIST

2ND JUNE, 1943

THE following are the names of medical men, and others associated with medical institutions, in the Indian Honours List of date 2nd June, 1943. We offer them our congratulations.

C.I.E.

Colonel (Temporary Brigadier) H. C. D. Rankin, O.B.E., V.H.S., R.A.M.C., Deputy Director of Medical Services, General Headquarters, India.

Rai Bahadur Anil Chandra Banerjee, Director of Public Health, United Provinces.

O.B.E. (Civil Division)

Major R. T. Hicks, I.M.S., Civil Surgeon, Cuttack, Orissa.

C. G. Pandit, Esq., Director, King Institute, Guindy. Lieutenant-Colonel J. M. Shah, M.B.E., I.M.S. (Retd.), Superintendent, J. J. Group of Hospitals, Bombay.

M.B.E. (Civil Division)

Captain J. Brebner, I.M.S., Civil Surgeon, Chittagong, Bengal.

K. Mitra, Esq., Officer-in-Charge, Nutrition Scheme, Bihar.

M. J. Quraishi, Esq., Colonel in the State Forces, and Chief Medical Officer, Rampur State.

Kaisar-i-Hind Gold Medal

Miss Marjorie Wilhelmina Jesson, Secretary, St. Stephens Mission Hospital, Delhi.

G. F. Scudder, Esq., Scudder Memorial Hospital, Ranipet, North Arcot District, Madras.

Kaisar-i-Hind Silver Medal

Miss Tehmina Kaikushru Adranvala, Matron, J. J. Group of Hospitals, Bombay.

Miss Jean Benzie, Doctor-in-Charge, Farrer Hospital, Bhiwani, Hissar District, Punjab.

Miss Marie Eleanor de Lorey, Health Visitor, Chittagong Maternity and Child Welfare Centre, and acting Matron, Chittagong General Hospital, Bengal.

Miss Elsie Irene Jacob, Lady Superintendent of Nursing, Medical College Hospitals, Calcutta.

Mrs. Beatrice Mary Spencer, Lady District Superintendent, St. John Ambulance Nursing Divisions, Calcutta.

R. C. Thanawalla, Esq., Medical Practitioner, Sholapur, Bombay.

Kaisar-i-Hind Bronze Medal

Mrs. Lakshmi Sachithanandam, Medical Practitioner, Cocanada, East Godavari District, Madras.

C. K. Naicker, Esq., Health Inspector, Madras.

K. C. Tripathi, Esq., Sub-Assistant Surgeon, Municipal Dispensary, Cuttack, Orissa.

Rai Bahadur

Captain N. N. Ghosh, Superintendent, Midnapore Central Jail, Bengal.

Rai Sahib A. N. Das, Assistant Director of Public Health, United Provinces.

J. Behari, Esq., Medical Practitioner, Allahabad, United Provinces.

P. C. Kacker, Civil Surgeon, Gorakhpur, United Provinces.

J. N. Bal, Esq., Civil Surgeon, Purnea, Bihar.

Rao Bahadur

B. T. Krishnan, Esq., Principal and Professor of Physiology, Medical College, Madras.

R. A. Adishesan, Esq., Director of Public Health, Madras.

B. T. Rao, Esq., Professor, Ear, Nose and Throat Diseases, Surgeon, Ear, Nose and Throat Department, and lately Superintendent, King George Hospital, Vizagapatam, Madras.

Rao Sahib C. R. Mankad, Medical Officer, Government House, Bombay.

K. M. Godbole, Esq., Civil Surgeon, Nimar, Central Provinces and Berar.

Shifa-ul-Mulk

Hakim K. Shams-Uddin, Member, Board of Indian Medicine, United Provinces, Lucknow.

Khan Sahib

S. I. H. Rizvi, Esq., Civil Surgeon, Hamirpur, United Provinces.

T. M. Khan, Esq., Air Raid Precautions Officer, Mardan, North-West Frontier Province.

M. A. H. Khan, Esq., Resident Medical Officer, Irwin Hospital, New Delhi.

Rai Sahib

K. K. Roy Chowdhury, Esq., A.R.P. Medical Staff Officer, Cawnpore, United Provinces.

B. Kishore, Esq., Honorary Secretary, St. John's Ambulance District Centre, Allahabad, United Provinces.

K. Chand, Esq., Chairman, Municipal Board, Almora, United Provinces.

S. K. Sahay, Esq., Assistant Surgeon and Radiologist, Patna Medical College Hospital, Bihar.

S. Lal, Esq., Member of His Highness the Raja of Mandi's Executive Council.

Rao Sahib

D. G. Reddi, Esq., Professor of Pathology and Vice-Principal, Medical College, Madras.

K. K. Shenai, Esq., Health Officer, Madras Public Health Service, Madras.

K. V. Nayak, Esq., Pathologist, King Edward Memorial Hospital, Secunderabad.

K. G. Palkar, Esq., Medical Officer, Civil Hospital, Sadra, Sabar Kantha Agency.

O.B.I.

To the First Class with the Title of 'Sardar Bahadur' Indian Army Medical Corps

Subedar-Major Dinesh Chandra Sen, Bahadur, O.B.I. Subedar (Hon. Subedar-Major) Amar Nath Puri, Bahadur, O.B.I.

Subedar-Major Lal Singh, Bahadur, O.B.I.

Subedar-Major T. B. Karumbayram, Bahadur, O.B.I.

Subedar-Major and Honorary Lieutenant Muhammad Hasan, Bahadur, O.B.I.

Subedar-Major Bagh Singh, Bahadur, O.B.I.

Subedar-Major and Honorary Lieutenant Sitaram Vishnu Sathe, Bahadur, O.B.I.

Subedar Chiman Rao Anand Rao Doctor, Bahadur, O.B.I.

Subedar-Major Hanmant Dattatrya Bedekar, Bahadur, o.s.i.

To the Second Class with the Title 'Bahadur'

Indian Army Medical Corps

Subedar Sudhireswar Sen Gupta, I.D.S.M.

Subedar-Major Guran Ditta.

Subedar Jogendra Nath Khan.

Subedar-Major and Honorary Lieutenant Shankar Krishna Gole.

Subedar-Major and Honorary Lieutenant Bhupendranath Lahiri.

Subedar-Major Sansar Chand.

Subedar-Major and Honorary Captain Abdul Wahid.

Subedar-Major Ananda Gopal Bandyopadhyay.

Subedar-Major Buta Mal.

Subedar-Major Vasant Sakhararam Gaikawad.

Subedar Rao Sahib Chingleput Manickam.

Subedar Jawand Singh.

Subedar-Major Prem Singh.

Subedar Udham Singh.

Subedar Karim Bakhtish.

Subedar-Major Dattatraya Keshav Rao Chitnis.

Subedar Srinivas Balasundaram Mudaliar.

Current Topics

Measuring Sulphonamide Activity

(From the *Lancet*, Vol. II, 22nd August, 1942, p. 223)

THE dosage of chemotherapeutic agents depends on a large number of factors, many of which relate to the host. Even their in-vitro action, however, varies greatly under different conditions, and not long ago it was counted an achievement to demonstrate any in-vitro activity in many agents of proved therapeutic value. With sulphonamides, the factors governing in-vitro activity have now been largely disentangled. The effects of different media have been allocated to definite antagonistic substances, of which *p*-aminobenzoate is the principal one. These are now recognized not as extraneous factors sent to plague the chemotherapist but as fundamental to the action of the drugs. The sulphonamides are bacteriostatic because they are sufficiently similar in structure to *p*-aminobenzoate to oust it from the essential bacterial enzymes which use it. This functional relationship to *p*-aminobenzoate has now been used to give numerical values to the activities of the different sulphonamides. The ratio S/P, where S represents the concentration of a sulphonamide necessary for bacteriostasis in the presence of different concentrations P of *p*-aminobenzoate, is almost constant for a given sulphonamide and a given organism, and is a measure of the purely antibacterial action of the drug. The smaller this ratio—that is, the smaller the quantity of drug needed for bacteriostasis—the more affinity does the drug have for the system it is disturbing. Such ratios have now been determined for various organisms and drugs; they have been referred to as antibacterial indices, or as measuring bacteriostatic potency, and their reciprocals have been called bacteriostatic constants. They are formally related to Ehrlich's chemotherapeutic index, though the connection is by computation and not yet by experiment.

The results of Wyss and others, given in the table, indicate that to both sulphanilamide (the least active drug) and sulphathiazole (the most active) the susceptibilities of seven organisms were in practically the same order; the ratio between the indices for the two drugs were much the same with each organism. Thus, as Green and Parkin point out on our opening page, it is fallacy to think that a particular sulphonamide is specific for a particular organism: the most active drug against one organism is normally the most active against all. All workers agree in principle with these results but give different numerical values for the antibacterial indices, almost certainly because they adopt different conditions of growth and different criteria of bacteriostasis. Thus Wyss and his colleagues observed the quantity of drug necessary to reduce bacterial growth in 16 hours to half its normal amount. Wood judged by the absence of visible growth during 5 days and therefore placed sulphadiazine equal in activity to sulphapyridine, while Rose and Fox agree with Wyss in putting the activity of sulphadiazine equal to that of sulphathiazole. Of the conditions of growth which affect the indices, Schmelkes and others have shown

pH to be of fundamental importance, and have demonstrated that the increase in potency of all sulphonamides with increase in pH is in accord with other evidences that the actual functioning part of a sulphonamide is an anion. In solutions of different sulphonamides whose strength is adjusted to give equal activity, the concentrations of anions are of the same order of

magnitude. It is apparently the group —S—NH_2 which stimulates —C=O at the drug receptor. Thus

differences between the antibacterial indices of the sulphonamides for a given organism largely depend on the amount of anion in their solutions.

In the clinical use of sulphonamides many more factors—differences in solubility, in absorption, detoxication and excretion by the host and even in availability and cost—must be taken into account in choosing the drug best suited to a particular purpose. For instance, we choose sulphaguanidine to attack intestinal organisms although its in-vitro activity is low. On the other hand, in the choice of sulphathiazole for staphylococcal and mixed infections antibacterial index is the overriding consideration. Thus although studies in-vitro cannot include all the factors which have to be considered in practical chemotherapy, yet with the present use of defined media they are giving us fairly accurate information of great practical value. Animal experiment, it must be remembered, introduces new and unknown factors to the study of human infections.

		DECREASING ACTIVITY					
DECREASING SUSCEPTIBILITY		Sulphathiazole	Sulphadiazine	Sulphapyridine	Sulphacetamide	Sulphaguanidine	Sulphanilamide
	<i>Bact. coli</i>	27 (36)	43 (100)	450 (100)	534 ..	3960 (1000)	2000 (1610)
	<i>Bact. aerogenes</i>	45	3220
	<i>Proteus vulgaris</i>	55	4000
	<i>Staph. aureus</i>	53	92	416	534	4570	4660
	<i>S. typhimurium</i>	92	6650
	<i>B. acidophilus</i>	133	8000
	<i>Ps. pyocyanea</i>	184	13330

ANTIBACTERIAL INDICES OF SULPHONAMIDES

Compiled from Wyss *et al.* and Wood. Wood's values are in parenthesis. The figures for different organisms are in the main comparable, but not entirely so because conditions of growth were not in form.

Complement Fixation in Typhus Fever Group

(From the *Lancet*, Vol. II, 10th October, 1942, p. 432)

THOUGH the Weil-Felix reaction with *Proteus* OX19 may indicate the presence of a rickettsial disease, it does not differentiate between typhus and Rocky Mountain spotted fever. Since the clinical differentiation between these diseases is very difficult the only means of diagnosis in the past has been the inoculation of guinea-pigs with blood from the patient immediately it has been withdrawn. Many unsuccessful attempts at complement fixation have been made with various antigens such as alcoholic extracts of organs of fatal cases, extracts of infected lice, infected guinea-pig tissues and infected tick eggs. Probably all were unsatisfactory because an insufficient number of rickettsias was present. In 1936 Castaneda obtained positive complement-fixation in cases of active and past infection with Mexican typhus and Brill's disease, using rickettsia from x-rayed rats infected with endemic typhus. A prolific source of typhus rickettsias was made available by Cox's discovery of their ready cultivation in the yolk sac of the developing chick embryo. Bengston has used as an antigen rickettsia grown by this method in a specific complement-fixation reaction for 'Q' fever and endemic typhus. Bengston and Topping have more recently demonstrated that the test will clearly differentiate between endemic typhus and Rocky Mountain spotted fever. Using an antigen prepared from endemic typhus, they found that in a case of laboratory infection the complement-fixation reaction was positive to a titre of 1/8 on the 10th day, rising to 1/4096 on the 15th day, and then dropping slowly to 1/512 on the 180th day. The Weil-Felix reaction was positive in a dilution of 1/80 on the 6th day and 1/320 on the 9th day, but fell more rapidly. In 53 cases of past infection the titre was 1/16 or higher even as long as 5½ years later. In contrast, 18 specimens from 14 cases of active Rocky Mountain spotted fever were all completely negative. Now Plotz and Wertman have confirmed the usefulness of the test by using an antigen of Rocky Mountain spotted fever rickettsia grown in tissue cultures, using the semi-solid agar method in Kolle flasks. Sera from 9 cases of Rocky Mountain spotted fever all gave positive complement-fixation. The earliest positive serum was obtained on the 12th day of illness with a titre of 1/24, and the serum of the oldest case who had had the disease 4½ years previously was positive in a dilution of 1/12. All sera from patients who had had Brill's disease or various other illnesses were completely negative. A corresponding result was obtained with sera from infected guinea-pigs. Though more or less specific for the typhus group of fevers, the Weil-Felix reaction being an indirect test has never been happily accepted by many workers. These new antigens may give us a simple inexpensive direct test for diagnosing this group of diseases. It will be interesting to learn if the complement-fixing antibodies are related to the neutralizing antibodies. If the two antibodies are comparable this will offer a simple means of testing the efficacy in humans of the various anti-typhus vaccines in use.

Nicotinic Acid in Treatment of Angina Pectoris

By F. J. NEUWAHL, M.D., L.R.C.P.E., Ph.D.
(From the *Lancet*, Vol. II, 10th October, 1942, p. 419)

THE use of nicotinic acid in the treatment of pellagra has achieved much prominence in the last few years, especially in the United States. In view of the advantages claimed for this substance in pellagrous psychosis, it was decided that a trial of its possibilities should be made with patients whose mental symptoms were of a similar, though not completely corresponding, type. These investigations have led to the present work. Six cases of angina pectoris have been treated with nicotinic acid, and the results in this series appear to be remarkably uniform and lasting.

Administration of the drug by mouth caused in several cases a noticeable decrease in number and severity of attacks, but in others the effect was transient, possibly because of interference with absorption or interaction of chemical substances in the gastric secretion. Moreover the drug could not be discontinued without relapse, and the treatment appeared therefore to be merely symptomatic. Intravenous administration heightened the efficacy of the drug. It was therefore decided to discard tablets of nicotinic acid, in order to obtain equal conditions for each case and an evaluation of the treatment after its discontinuation. A drip infusion of a 0.05 per cent solution of nicotinic acid was chosen to overcome differences in susceptibility to nicotinic acid; isotonic solutions are rapidly absorbed, giving sufficient concentration of the medicament in a short time. One 100-300 mg. produced as a rule a result, which was maximal after 12-24 hours. Further infusions seemed to cause a definite stabilization in the condition of the patients, who became free from anginal attacks after several weeks, the worst cases reacting best. In most cases it was considered sufficient to give six infusions, so that treatment finished after approximately 3 weeks, though in some cases more treatment may be required. We now have 6 cases showing complete or almost complete regression of symptoms of angina pectoris over a period of 3-7 months after completing the course of treatment; 3 cases have actually resumed heavy manual work.

CASE-RECORDS

Case 1.—A builder, aged 65, who had always been healthy until the first attack of substernal pain 2 years ago. Continued to work with the help of nitroglycerin tablets. The pain, constricting and burning in type, radiating into both arms, became gradually worse, especially in cold weather. In autumn, 1941, frequent attacks of pain caused him to retire from work. No dyspnoea at rest, but slightly breathless on exertion. Physical examination of the heart did not reveal any enlargement, sounds faint, no murmur; resting BP 120/80 mm. Hg. Pulse regular, 84 per minute, radial and retinal vessels appeared normal. He was tested to ascertain the amount of effort necessary to cause anginal pain; 17 steps of the usual type of staircase caused intense pain, with BP 180/110 mm. Hg., pulse 110. Treatment started 2nd February, 1942. Next day reduction in pain was noticed, and patient felt able to walk a short distance; after the 8th infusion on 21st March, he could dig a plot 10 ft. by 20 ft. in his garden in less than an hour without pain. After the 10th treatment he was tested again; 193 steps of the same staircase were mounted, going very quickly up and down. This exercise was interrupted because no pain was felt, and it appeared unnecessary to continue the test. When re-examined on 7th July, 1942, he was doing the work of a man in good health, did not take any drugs, and had no pain, though he carefully abstains from sudden exertion.

Case 2.—A cotton spinner, aged 50. No history of serious illness. Started to become breathless on exertion 8 months ago; 2 months later had acute attacks of heartburn and indigestion, especially after an effort. He took alkaline powders, and they helped to a certain extent. Again 2 months later, after a brisk walk, had intense substernal pain and had to stop. This pain forced him to give up work, because it reappeared frequently from that time after exertion. Examination on 10th March 1942, showed no dyspnoea at rest, but breathlessness on exercise. No signs of congestive failure or cardiac enlargement; heart sounds faint. Systolic murmur over base of heart. No abnormality of peripheral and retinal vessels. Pulse 90 per minute. Resting BP 130/90 mm. Hg. Wassermann reaction negative. No signs of renal defect. On mounting a staircase, 38 steps caused an anginal attack, which forced him to stop. BP shortly afterwards, 170/70 mm. Hg., pulse 96 per minute. Nine minutes later, at 4-24 p.m., infusion was started, BP fell from 135/75 to 118/80 mm. Hg. Pulse-rate fell from 90 to 68, but later remained about 78 per minute. Infusion finished at

5-40 p.m. At 5-45 the patient was retested; 95 steps of the same staircase were mounted very quickly. Became breathless, but did not experience any pain at the end of this exercise. Next day was tested by a walk of $\frac{1}{2}$ mile, slightly uphill. Became very breathless but felt no pain. Three infusions were given. He felt fit after this treatment, and has since resumed work. Re-examined on 24th July, 1942. Has been employed at his former job for the last $3\frac{1}{2}$ months. Does hard work every day, but abstains from sudden exertion, has not experienced any pain, and feels extremely fit.

Case 3.—A farm hand, aged 27, with congenital syphilis. No external signs of syphilis. Never been seriously ill and is in fine physical condition. WR ++. Examination of CNS entirely negative; no signs of heart-failure; no dyspnoea on exertion; no enlargement of heart and no murmur; second aortic sound slightly accentuated. Pulse irregular, 76 per minute, BP 130/80 mm. Hg. Came under observation on account of unbearable pain in chest, radiating down inner side of left arm, and once into both arms. First attack occurred in July 1941, after effort. On two occasions pain became unbearable, and he had to lie down and keep immobile for 5 minutes before it ceased. Left arm was sore during and after attacks of pain, which usually lasted 4-5 minutes, unless interrupted by a nitroglycerin tablet. Received antisyphilitic treatment, starting with small doses of iodine and bismuth. Later neoarsphenamine was given and well tolerated. No change in the anginal syndrome. Treatment with nicotinic acid started 23rd January, 1942. Soon after first infusion reported a decrease in pain during attacks. After three infusions took up work again, and has remained a very active worker. Has no pain except when starting a sudden and sustained effort. Even then he has not to stop but only to slow down to get relief. It seems evident that the orifices of the coronary arteries have been narrowed by a syphilitic process and the anginal pain therefore returns when the structural changes do not allow a sufficient amount of blood to enter or to leave the coronary system.

Case 4.—A bus driver, aged 58. Was forced to give up work 5 years ago on account of mitral stenosis. Very dyspnoeic on slightest exertion; has a persistent irritating cough. Radial vessels slightly harder than normal. Pulse irregular (frequent extrasystoles). At times pulse grossly irregular, due to transient auricular fibrillation. BP 180/110 mm. Hg. In 1938 experienced first substernal pain. Afterwards attacks came on at any time after slight exertion and after food. When mild they had the character of acute indigestion and fullness in the chest, when stronger a burning pain radiated into both arms, especially down the inner side of left arm. First treatment 4th February, 1942. Morning after infusion was able to rise without pain and to start dressing immediately, instead of sitting on the edge of the bed to overcome the first anginal attack. Received six infusions within 3 weeks. Has had no further anginal attacks. Now works in his wife's business, can walk 5 miles, and is generally active and independent.

Case 5.—A widow, aged 62. Was a cotton spinner until 2 years ago, since when has not worked because of pain in chest, which became gradually worse, was burning in character radiating into left arm. Pain easily caused by short walk or by exercise after a meal. Worse in cold weather. No dyspnoea at rest, but breathless on exertion. Physical and x-ray examinations show only moderate enlargement of heart, but well-marked dilatation of aorta. Blowing diastolic murmur in aortic area. Water-hammer pulse. Radial and retinal vessels slightly tortuous. WR negative. Resting BP 135/85. After first infusion on 4th May, 1942, much better nights. Acute attacks of pain disappeared entirely, but still felt oppression in chest during long walk. After third infusion this oppression also disappeared. Now undertakes much more exercise, and has regained her old confidence. Tested on a walk, approximately 1 mile, going slightly uphill: no pain but tired and breathless.

Case 6.—A gardener, aged 60. Illness started in May 1941, with attack of breathlessness on exertion. Stayed off work for a week. Shortly afterwards had acute attack of pain in chest while lifting window of a greenhouse. Attack was severe, lasting for a long time, and only passed slowly away on sitting down. Left arm remained sore for long time afterwards. Since then pain has frequently recurred. Only caused by exertion, is continuous, and passes away when he rests. It is of burning and gripping type. Not breathless at rest; no signs of cardiac failure or of a vascular lesion. Heart shows neither clinical nor x-ray signs of enlargement. Peripheral and retinal vessels slightly thickened and tortuous. WR negative. Resting BP 165/90 mm. Hg. Pulse-rate 84. Average number of steps of usual type of staircase required to produce pain was 60. BP afterwards 210/110. Pulse-rate 120. Abnormally breathless. First treatment 10th March, 1942. Improved considerably. Retested after third infusion on 27th May. Amount of exercise tolerated now limited by breathlessness, not by pain. Has had no anginal attack since first infusion, sleeps much better, has taken up light work again, and regained some of his old confidence, though he still abstains from exertion.

PHARMACOLOGY

Most of the clinical work with nicotinic acid, apart from pellagra, was based on its vasodilating action, which appears to be independent of its action as a vitamin. This effect is, however, of short duration, and elimination of the drug by the body is probably completed within a few days. To account for the lasting results in the foregoing cases, we have compared the action of nicotinic acid with that of histamine, both of which have a heterocyclic ring—N— with a substituent group in beta position. Though there is no obvious chemical relation, a resemblance between the pharmacological action of histamine and nicotinic acid was found.

The well-known reactions following a subcutaneous or intravenous injection of 0.1 mg. of histamine sodium phosphate can be nearly reproduced by a 50-500 times larger quantity of nicotinic acid. The effects of such a dose of nicotinic acid are as follows:—

On smooth muscle.—No effects in normal persons, except in two who complained of severe cramp-like pain in the epigastrium after 5 mg. of nicotinic acid intravenously. A delayed action was noted in 3 asthmatics; 2 reported severe asthmatic attacks after taking 50 mg. of nicotinic acid by mouth, the third, who received 100 mg. by intravenous infusion, reacted with a violent attack 15 hours later. In 4 other cases, however, the effect appeared so beneficial that ephedrine was replaced by nicotinic acid.

On secretion.—Rise in the volume and acidity of the gastric secretion after 50 mg. of nicotinic acid intravenously. In 2 patients with a fasting achlorhydria, hydrochloric acid appeared in increasing amounts, though the effect was not so great as that produced by histamine. Sweating was never noticed, even with doses of 600 mg., though Forgan (1939) mentioned this action.

On cerebrospinal fluid.—Slight rise in pressure.

On blood-vessels.—Moore (1940) reports that nicotinic acid produces vasodilatation and increased blood-flow in the brain and spinal cord of the cat. Furtado confirmed the cerebral vasodilator action of nicotinic acid. Adams and Robinson (1941) utilized the vasodilatory effect of nicotinic acid with success in 7 cases of trigeminal neuralgia. A headache similar in type to that following an intravenous injection of 0.1 mg. histamine could be produced in 4 patients. It was necessary to give the infusion rapidly. A sense of fullness is first felt, which increases to a sharp headache.

On the heart and blood-vessels.—The responses to a given dose vary in different subjects, and in the same subject from day to day. Because of these variations, every observation has been followed by several control tests, to test and possibly to eliminate the effect of a modifying factor on pulse-rate and blood-pressure. Healthy adults are far less affected than patients,

especially those with hypertension. Usually the effects begin within 1-2 min. of the start of the infusion, simultaneously with the flushing of the face and the upper part of the body; the systolic blood-pressure falls 5-40 mm. Hg. The diastolic pressure was little altered, but sometimes rose a few mm. The striking fact which emerges from these observations is the difference between histamine and nicotinic acid in their action on the heart-rate. The former causes a distinct increase, the latter in most cases an equally distinct slowing. The reduction coincides in each case with a fall in blood-pressure, and this relationship cannot be accidental, because it occurred in more than 100 infusions and 40 different patients, though in an equal number of normal controls the results were less definite.

DISCUSSION

The degree of central vagal tone, which exerts a prevailing influence on the heart-rate, runs parallel with the height of the blood-pressure. Nitrites, like histamine, cause a well-marked fall in blood-pressure, and thereby an acceleration in pulse-rate, the action on the vagal tone being a sequel to the change in blood-pressure, and only to a slight degree a direct action on the vagus itself. The question therefore remains how nicotinic acid can cause a fall in blood-pressure, and at the same time a slowing of the heart-rate. One possibility is that nicotinic acid causes a vagal stimulation. This view however implies that production of acetylcholine follows the administration of nicotinic acid, because the vagus produces its effect on the heart by liberating free acetylcholine at its endings. Comparison of nicotinic acid and acetylcholine, by measuring their effect on the frog's heart and rectus abdominis, shows that nicotinic acid has scarcely any effect, and a physiological relationship between the two substances appears unlikely. A second possibility is that nicotinic acid causes a rise of pressure in the cerebral arteries and an increased blood-supply to the brain. Furtado quotes C. D. Aring, who found that nicotinic acid produced an increase in cerebral circulation, accompanied by intense cerebral congestion. The rise of pressure could bring about inverse changes in the arteries of the rest of the body, and, accompanied by reflex cardiac inhibition, would account for the fall in blood-pressure and the slowing of the heart-rate.

SUMMARY

A series of 6 cases of angina of effort have been treated by intravenous infusions of nicotinic acid. Subjective and objective evidence of continued improvement followed and this has been maintained during the last six months. The action of nicotinic acid on blood-pressure and heart-rate was constant in almost every case, both being reduced.

Crushing Injury

By E. G. L. BYWATERS, M.B., M.R.C.P.

(Abstracted from the *British Medical Journal*, 28th November, 1942, p. 643)

In the heavy air raids on London in the autumn of 1940 we attended some patients who had been pinned for several hours underneath the debris of their own bombed houses. Shock was present, which responded adequately to transfusion: the limb which had been compressed was found to be swollen and sometimes pulseless. To our surprise these patients developed renal failure with casts in the scanty urine, and died in uræmia about the seventh day. This appeared to us at that time a new entity: it was described as such under the title of 'Crush Injuries with Renal Impairment'. Since then, however, we have discovered descriptions of it by German authors from the war of 1914-18. During that war Frankenthal and others directed attention to the local muscle damage, and it was not until later that the renal lesion was adequately emphasized. The condition had actually occurred in 1909 in people buried beneath the debris of the Messina earthquake, but as the relief expedition arrived on the

scene a fortnight after the eruption, only the survivors with gangrene of soft parts were seen.

Apart from German books on military surgery we have found no other references to it and no further records of cases. This is curious, since, even apart from the almost continuous warfare since 1918 somewhere in the world, such accidents do occur in the mining industry and have recently been described. Since the first few cases in air-raid casualties were published, the condition has been generally recognized here. Hospitals in the Emergency Hospital Scheme of the Ministry of Health have been asked to notify cases to the Medical Research Council, which now has records of over 70 cases. It is on this group through the kindness of the Council and its observers throughout the country, that the following observations are based. About 5 per cent of air-raid casualties in an urban area may be of this type.

CLINICAL DESCRIPTION

The patient has usually been pinned by the limbs beneath heavy beams or pieces of masonry for a period of several hours. If seen soon after release from this compression he generally appears comparatively well, apart from other coincidental wounds, fractures, etc. Soon, however, he enters the first phase of shock, due to loss of plasma through the damaged capillary walls into the extravascular tissue spaces of the affected limb, which becomes swollen. As a consequence, the hæmoglobin and corpuscular content of the blood rise relative to the plasma, and vasoconstriction occurs to compensate for the decrease in circulating blood volume. During the first phase the skin is pale, cold, and moist, but the blood pressure is maintained at a nearly normal level. Later, however, vasoconstriction may become unable further to compensate for this leakage of plasma into the damaged area; the blood pressure then falls rapidly. This is the second phase of shock. If fluids such as serum, citrated plasma (plain or recalcified), and blood are given intravenously at this stage in adequate amounts the blood pressure can be restored to normal levels. This is the phase of recovery from shock. There may, however, be failure to respond to intravenous protein-containing fluids if the blood pressure has been allowed to remain at too low a level—below 80 mm. Hg.—for too long a time.

Thereafter the general condition of the patient causes no anxiety until the first or second urine passed is noted to be bloody and to contain a pigment in solution similar in many ways to hæmoglobin and giving a positive reaction to the benzidine peroxidase test. The urine also contains albumin, creatine, pigmented granular casts, and sometimes pigmented granules somewhat resembling erythrocytes; it is highly acid (pH 4.6 to 6.0). The daily output of urine may become very small despite an adequate fluid intake, but the pigment disappears as a rule after the second day.

Meanwhile, however, the damaged limb has swollen, is hard, tense, and cannot be indented. This swelling is usually progressive for the first four or five days, except possibly in cases associated with blood-vessel damage. The skin shows small petechial hæmorrhages, erythematous weals, and large blisters, related to the areas of direct contact pressure. These blisters are often thought to be the results of burns. They are not. They may occur in crops, related in time to the return of circulation to the damaged part. There is anæsthesia of the limb, often of a patchy distribution due to damage of the terminal nerve fibres, and sometimes of a nerve-trunk distribution. Paralysis, which may be of any severity, is usually present; in many cases, arterial pulsation in the peripheral part of the limb is absent, the limb is cold and pale, and the onset of gangrene is to be feared. It is important to record the state of the circulation, which can be followed from time to time with the oscillogram. Sometimes Art and sometimes Nature will restore the circulation; often then the pulsation is greater on the damaged than on the sound side. Whether gangrene sets in or not, the severely damaged patient will continue in a peculiar state of mental apathy, alternating with phases of

anxious and apprehensive awareness of his condition, until the end of the first week. During this time vomiting is a prominent symptom, and the blood pressure gradually rises to a level much in excess of the normal. The blood urea, potassium and phosphate concentrations rise progressively, and the CO₂-combining power of the plasma falls. The urine flow is greatly diminished and, despite the high blood urea, there is failure of the tubules to concentrate urea and other solids, and also failure to reabsorb chloride, even though the blood chloride concentration is low: tubular dysfunction is therefore indicated. Pain in the loins (possibly evidence of stretching of the renal capsule) occurs not infrequently about the fourth or fifth day. Some patients have had severe abdominal pain and rigidity, and have been opened without anything definite being found. This symptom may be related to the kidneys.

The end of the first week is the critical period: in those patients who recover, a sudden diuresis is seen, and thereafter the urinary output will rise gradually to very high levels. At the same time the blood urea level falls; the urea clearance test (of van Slyke) may show improvement of tubular function, although this may not reach the normal level until several months after the injury. During recovery, granular and epithelial casts may be noted from time to time in the urine. In the damaged areas, skin and muscle may slough away: infection may occur. This is the 'pressure necrosis' observed in base hospitals when the initial phases of the syndrome have passed unnoticed. Restitution fibrosis may occur if the damage is slight, a condition resembling Volkmann's ischaemic contracture.

In more severely damaged patients at this critical period, some cardiac irregularity may be noticed, and electrocardiograms taken at this time show changes not unlike those seen in experimental potassium poisoning. The serum potassium level may be greatly increased, but it is difficult to say whether it is high enough to cause symptoms. Too little is known about the balance between intra- and extra-cellular potassium at increased blood levels to be dogmatic on this point. However, we know that potassium is very soon and very easily lost from damaged muscle and that it cannot be adequately excreted if there is severe renal impairment. Hoff *et al.* are of the opinion that, in man, death in uraemia from ordinary causes associated with a high terminal potassium is not a 'potassium death', because the kidney can excrete this substance even in extreme oliguria. If, however, there is an increased flow of potassium into the blood stream from intracellular sources (and, in general, intracellular potassium is about 10 times as concentrated as extracellular potassium) it seems possible that this substance may be exerting toxic effects. Measures, such as insulin injection, directed towards the storage of circulating potassium might be found of value in cases in which there are indications of recovery of renal function.

Death occurs very suddenly: the patient may call out in great alarm, and be found pale and sweating, with dilated *alae nasi*. He may die within one or two minutes, or recover until a similar episode an hour or so later finally terminates his life.

PATHOLOGY

Changes are seen in the adrenals, muscle, vessels, and skin, and in the kidneys. There may be other traumatic lesions, such as fat embolism, contusion, or blast lung. The muscles show one or more of the following types of change:—

1. Part of the muscle is blanched, unduly friable and necrotic, resembling fish flesh. The sharp demarcation line corresponds to the skin-pressure areas. This type is due to direct-pressure ischaemia.

2. The whole of the muscle is white and necrotic. This is usually seen in those muscles contained within tight fascial compartments, and it is thought that this necrosis may be due to rise of pressure within the compartment, with subsequent necrosis. It is for this type that fascia-splitting operations have been proposed.

3. The muscle may appear grossly normal, without pallor, but patchy necrosis of isolated fibres may be seen microscopically. It is this type that is associated with arterial spasm, due perhaps to periarterial haemorrhage or direct arterial damage, and sometimes associated with rupture of a main limb vessel without any prolonged crush. This type is thought to be due not to direct-pressure ischaemia but to vasogenic ischaemia. These changes depend upon the survival time and upon the extent of circulatory return.

The kidneys are enlarged and swollen (except in patients dying early); they may show a white zone in the cortex, which is wet and glistening. Microscopically, the collecting tubules and the distal convoluted tubules contain a brown pigment material even in patients dying within one or two days of the injury: the paroxysmal convoluted tubules show cloudy swelling and desquamation. In cases surviving for three to four days, further changes are seen consisting of areas of necrosis in the boundary zone and in the neighbourhood of distal convoluted tubules in the cortex. These are usually pronounced in the typical case ending fatally at the end of the first week from renal failure: there is oedema and cellular proliferation surrounding the large hyaline casts which are protruded into the interstitial tissue in these regions. Some polymorph infiltration may be seen within the collecting and distal convoluted tubules. The glomerular capsule may show cuboidal epithelium. This appearance is not entirely specific, since it occurs in certain other conditions. For instance, such casts, composed of haemopigment, occur after intravascular haemolysis if the plasma haemoglobin exceeds the renal threshold of 135 mg. per 100 c.cm. One of the most common causes of haemoglobinuria nowadays is mismatched transfusion. Not only is the morphologic lesion similar, with pigmented casts and, in certain cases, areas of focal necrosis, but the clinical course is also similar with anuria and death in uraemia.

PATHOGENESIS

At first it seemed we might be dealing with some such haemolytic reaction, since our first cases had had serum and blood transfusion, but there were three reasons why this appeared improbable. Firstly, the blood used was group O; secondly, there was no clinical evidence such as chill, rigor, headache, limb pains, vomiting, or jaundice following transfusion, nor was there any increased colour in the plasma, such as one would expect if any serious haemolysis had occurred; thirdly—and this seemed the most cogent argument—no such reactions had occurred in any of our shocked and transfused casualties other than buried cases. Later we were to learn that this syndrome developed without any therapy other than 'rest and quiet'. Extravascular haemolysis, as in a haematoma, has been invoked to explain certain cases. In general, however, following extensive bruising of soft parts, the uptake of freed haemopigment is so slow that there is no rise above the renal threshold, and seldom even jaundice (except locally) unless there is associated liver dysfunction.

Discarding this theory, we were struck by the pallor of the damaged muscle at necropsy. Normal muscle owes its colour to a pigment called 'myohamoglobin', which differs from haemoglobin in several ways, since, although the iron-containing porphyrin group is the same, the globin portion is smaller. For instance, the spectral bands are 30 A.U. nearer the red, and the carbon monoxide span is 30 and not 60 A.U. There are three conditions in which myohamoglobinuria occurs; perhaps the best known is paralytic equine myohamoglobinuria. Five cases have been recorded in man, and we have seen a case recently, probably falling into this group: muscle necrosis is associated with myohamoglobinuria, renal damage, and an increased blood potassium after exercise. In this disease, in the Haff disease, and in epizootic myohamoglobinuria the muscles are blanched and are the seat of degenerative changes. The next step was therefore to identify this pigment in the urine. We were able to do this, using

the Hartridge reversion spectroscope and comparing the pigment with myohæmoglobin extracted from perfused human muscle. Dr. Rimington confirmed our findings, and in addition demonstrated another important characteristic. As the molecule is one-quarter the size of that of hæmoglobin, it will filter through smaller pores of semi-permeable membranes, and it will also sediment more slowly in the ultracentrifuge. Both of these things occurred, and they are of some clinical importance because they explain the curious fact that no pigment is seen in the blood stream; as the renal threshold is so much lower than that for hæmoglobin there is prompt excretion and no such accumulation in the blood stream as occurs with the latter pigment.

We regarded this identification of myohæmoglobin as important not because it might be the cause of the renal failure (although that is possible) but because, like the creatinuria it was associated with, it definitely incriminated muscle damage. Cases had been cited (often, however, poorly investigated) in which there was no evidence of tissue damage other than lacerations. Since then we have found that crush lesions of trunk muscles often go unnoticed except for this indirect evidence of myohæmoglobinuria. Cases do occur, however, in which muscle necrosis follows no direct compression ischæmia but ischæmia due to arterial spasm or rupture of main arteries, and these cases may also develop renal failure.

Was this pigment responsible for the renal failure? In the similar case of hæmoglobinuria with renal failure following intravascular hæmolysis the simplest theory is that the pigment blocks the tubules. Baker and Dodds demonstrated that, in acid urine with high salt content, the pigment changes to the less soluble acid hæmatin and is precipitated; with large and repeated doses under these conditions renal failure could be induced. Hence alkalization of the urine became the practice with all patients in whom a hæmolytic reaction was to be feared.

Certainly, in these crush cases, oliguria, due to shock, and an acid urine are seen and myohæmoglobin behaves similarly to hæmoglobin under these conditions. Animal experiment has shown that in the rabbit, whose muscles contain no myohæmoglobin, muscle necrosis reproduces all the signs and symptoms of crushing injury except myohæmoglobinuria and renal failure. When myohæmoglobin in a quantity comparable to that excreted in human crush cases was injected into the rabbit acidified with ammonium chloride, we were able to produce death from renal failure. It seemed possible that partial blockage brought about a rise of intrarenal pressure, and this in turn led to irreversible renal failure.

The proof of this theory will lie in the prevention of renal failure in man by administration of alkali. As yet the validity of the theory is undecided, and the exact mechanism by which muscle necrosis produces renal failure has not been fully explained.

ASSOCIATED FEATURES

Crushing injury is often associated with other lesions which complicate both the clinical picture and the treatment. Of these the most common is hæmorrhage, which may be internal or external. Hæmodilution occurs after a variable number of hours, and if hæmoconcentration due to plasma loss occurs at the same time the net change in hæmoglobin may be nil. Fat embolism often associated with fractures, may occur. The lung symptoms are manifest a few hours up to a day after the injury, and consist of pain in the chest, dyspnœa, pallor or cyanosis, and congestion. Systemic embolization occurs later on the second or third day, with fat globules in the urine, petechiæ, and a surly stupor or delirium. Thus uræmia has seldom an opportunity to develop unless the fat embolism is of a minor grade producing a delayed pneumonic process. Blast or concussion injury of lung is less common: it may be present as slight dyspnœa with frothy blood-stained sputum and a ruptured drum or, later, lobar pneumonia. Another condition sometimes met with is carbon monoxide poisoning.

DIFFERENTIAL DIAGNOSIS

Oliguria may be due to oligæmic shock alone, to dehydration from vomiting or inadequate intake, to blockage by acetyl-sulphapyridine crystals, or to a mismatched transfusion: examination of the urine and blood, investigation of the blood pressure, and an intake chart are necessary to differentiate these conditions. Cortical necrosis has occurred after traumatic injury to the liver with necrosis. This is very rare. There is often a temporary retention of urine, disclosed as such by the passage of a catheter.

Hæmaturia from direct injury and hæmoglobinuria from exposure to cold are differentiated by examination of the urine and the use of the spectroscope.

Limb-swelling may be due to a hæmatoma: the skin wheals are absent and there is no doughy feel to the muscle. Skin wheals may be mistaken for burns.

PROGNOSIS

The prognosis depends on many factors—first, on the amount of muscle necrosis. If comparison is for a shorter period than one hour the muscle survives unless arterial spasm prolongs the ischæmia. If longer than 4 hours, necrosis ensues. For periods between, tissue survival may depend on temperature. Curiously, periods of burial longer than 12 hours seem less serious than shorter periods, perhaps because only the least-hurt patients survive, perhaps because of a natural self-amputation and failure of the circulation to return to the part. The amount of necrosis in our animal experiments determined the height and duration of the hæmoconcentration. Once the patient has recovered from shock, renal damage decides the outcome. Arm crushes have a better prognosis than those of the leg, perhaps owing to the smaller amount of muscle. The presence of other injuries adversely affects the result; the rapidity with which treatment can be started probably also does. About one-third of 70 cases have recovered; these were mostly minor cases without severe shock or uræmia—a class of case that is being increasingly recognized. However, a case has been seen in which the blood urea rose to 470 mg., and yet, without any treatment at all, on the critical seventh day a diuresis occurred and was followed by recovery. Claims of successful treatment have therefore to be very fully substantiated.

Summarizing, the extent of injury, the degree of hæmoconcentration, oliguria, and blood urea rise constitute the four chief determining factors of prognosis.

Finally, one patient whom I saw through the kindness of Dr. Grant, whose patient he was, had drunk four pints of beer just before the establishment was demolished. They dug him out 11 hours later with both legs broken. In spite of a fairly high blood potassium level he recovered, but showed little hæmoconcentration or uræmia. The possible protective action of this beverage might be worth investigating.

TREATMENT

The natural tendency under emergency conditions is to treat shock first, then the local limb condition, and lastly the renal failure on or about the third or fourth day, when signs of renal damage are obvious. Since it is possible that the renal damage occurs soon after the re-establishment of an adequate blood supply to the damaged limb, these three aspects should be considered in the reverse order:—

1. Ample alkaline fluid (3 litres daily), by mouth preferably, or by rectum, intramuscularly or intravenously, must be given rapidly at the earliest possible moment, to produce an alkaline diuresis. If possible, this should be done while the patient is still trapped under the wreckage. We favour for ingestion an alkaline fluid flavoured with citrus juice or peppermint and glucose, containing sodium citrate and sodium bicarbonate, 3 g. of each to the ounce. Coffee or tea is also useful, and morphine should be given if required. For intravenous injection, isotonic sodium citrate (3.8 per cent) or sodium lactate (M/6) should be used. Enough alkali should be given to make the urine alkaline: this will mean probably 30 to 40 g.

daily or more by mouth, or a lesser quantity by intravenous injection. If tetany is induced, calcium gluconate should be given intramuscularly. Potassium salts must not be used. Sodium sulphate (2 per cent) may also be injected intravenously in combination with the above measures to maintain urine output.

2. With the kidneys thus protected, it is safe to restore the circulation by combating shock, if this is present. Plasma or serum should be given, or, if there has been much hæmorrhage, blood. A large quantity may have to be administered: so long as the arterial blood pressure remains low no harm need be feared. Saline is of no value. Overheating the patient is dangerous.

3. Local treatment to excise wounds and set fractures may now be undertaken. The limb may have to be amputated: if this possibility is considered on the first day it should be done soon, to prevent the absorption of autolytic products. A tourniquet may be useful. Amputation later may not save life, and should be done only if the limb is non-viable. Active measures to restore circulation in the damaged limb (only permissible once it is assured that there is an adequate alkaline diuresis) include elevation of the leg, incision of fascial sheaths, stripping of a damaged artery, or the use of alternate positive and negative pressure. Vasodilatation is best assured by giving alcohol and warming the body. The limb should be kept cool rather than hot, perhaps with bags of ice. This delays autolysis and decreases local metabolic needs in ischaemic tissue. Whether limitation of swelling by plaster-of-Paris, tight binding, or inflatable rubber bags will do more than limit plasma loss into the leg is uncertain. There is as yet no evidence that it will prevent renal damage.

It must be remembered that we are treating not only an injured limb but a human being who has passed through an exhausting and terrifying ordeal. Pain must be relieved and steps taken to see that the patient is comfortable in body and mind.

If by these means a fatal outcome, either from shock on the first day or from renal failure on the seventh, can be avoided, we have left a patient with severe muscle damage. These muscles may remain paralysed or may shorten, giving rise to Volkmann's contracture. They should be adequately splinted and exercised. If sloughing and gangrene occur, infection should be controlled.

In conclusion, this was until recently a little-known type of injury: we still know very little about its exact mechanism and how to treat it. Further observations on the effects of controlled and adequately followed treatment are needed.

The Blood-Brain Barrier

(From the *British Medical Journal*, Vol. II, 12th December, 1942, p. 703)

THE conception of a semi-permeable barrier between the blood and the brain dates back to the end of the last century, when it was found that certain substances such as trypan blue or diphtheria toxin failed to produce any change in the central nervous system (c.n.s.) on intravenous injection, while they were very active on intracerebral or intraventricular injection. In recent years there has been a growing interest in the practical application of this theory to medicine, and Friedemann has summarized the present position. It should perhaps be emphasized that the blood-brain barrier is located in the capillary endothelium of the cerebral vessels, and that the cerebrospinal fluid plays no part in this connection as an intermediary in the exchange of substances from blood to brain. The method of investigation may be illustrated by certain experiments on diphtheria toxin. It was found that the rat is almost immune to intravenous injection of this toxin while highly susceptible to intracerebral injection, which caused striking pathological changes; conversely, in rabbits the protective dose of antitoxin is the same by the intravenous or the intracerebral

route, although the toxin is 20 to 40 times more potent on intracerebral injection. These results suggest that the capillaries of the c.n.s. are relatively impermeable to diphtheria toxin, and so circulatory failure in the early stages of the infection, at least in animals, is probably not due to medullary paralysis. From similar experiments there is additional evidence that tetanus and botulinus toxins reach the c.n.s. by neural rather than by vascular pathways. Adrenaline caused a five- to ten-fold increase in the permeability of the cerebral capillaries to substances such as paraldehyde, strychnine, and ethyl urethane, to which they are already permeable. It was suggested that since adrenaline lowered the intravenous lethal dose of cobra venom for a rabbit from 0.5 mg. to 0.025-0.05 mg., the blood-brain barrier is therefore by analogy permeable to cobra venom. While this conclusion is not perhaps altogether justifiable, the observation is clearly of practical importance in so far as it can be applied to man. Friedemann also concluded that the blood-brain barrier was impermeable to the neurotropic viruses, such as those of poliomyelitis or rabies, which, like tetanus and botulinus toxins, must therefore reach the c.n.s. *via* the peripheral nerves. Experiments with tetanus and diphtheria antitoxins suggested that they could pass through the cerebral capillaries, but that the antitoxin concentration in the intercellular fluid was only 1/20 to 1/60 of that in the blood plasma. This observation is a further justification for the intrathecal administration of antitetanus serum in cases of tetanus, and explains the slow therapeutic response. Of the various drugs which act on the c.n.s. it was observed that many may act indirectly, as, for instance, by stimulating the carotid sinus. To be sure that they penetrate the blood-brain barrier it is necessary to identify them in the brain after intravenous injection. In this way it has been shown that many alkaloids and sulphonamides pass the cerebral capillaries, while neoarsphenamine and suramin (Bayer 205) do not.

Friedemann concludes from the large number of observations on this subject that the ability of substances to pass the capillaries of the c.n.s. is determined by their electro-chemical properties. So the higher permeability of the blood-brain barrier to electro-positive substances may explain the rapid action of cobra venom in contradistinction to the slow action of tetanus and botulinus toxins, which have to make their way along the peripheral nerves into the c.n.s. rather than *via* the blood stream.

Structure of Vaccinia

(From the *Lancet*, Vol. II, 8th August, 1942, p. 162)

SLOWLY some of the mysteries of the viruses are being unravelled while others tend to become more complicated. It becomes increasingly clear that their properties as viruses are so divergent that generalities must be avoided. They range in size from those of vaccinia, myxoma, canary pox, lymphogranuloma venereum and rabies, all between 125 and 175 μ in their largest diameter, down to poliomyelitis (human and mouse) at about 12 μ and foot-and-mouth disease at about 10 μ . The viruses of lymphogranuloma venereum and a new mouse pneumonitis virus are susceptible to the action of the sulphonamides and thus so far different from all the rest. Vaccinia, one of the largest and most highly organized of the viruses, has been intensively studied by Hoagland and his colleagues. They found that the elementary bodies of vaccinia are composed chiefly of protein, thymonucleic acid, lipid and carbohydrate in concentrations not much different from those found in bacterial cells. They have since found small amounts of biotin and riboflavin present. In purified suspensions they have also found a copper constituent in a concentration amounting to 0.05 per cent of the dry weight of the virus; a 25-fold increase occurring during purification of the virus. In contrast to this Sprince and Schoenbach have failed to demonstrate significant amounts of riboflavin, pantothenic acid and biotin in moderately concentrated solutions of purified tobacco

mosaic virus which is only about 1/5th the diameter of that of vaccinia. The elementary bodies of vaccinia have also been shown to respond to osmotic influences and to be antigenically complex. The use of the electron microscope has given new opportunities for observing any structural differences that may help to explain their action and differentiate between the bacteria and viruses. Von Borries and the Ruskas in their original experiment found the virus particles of vaccinia somewhat oval in shape and uniformly opaque. Green, Anderson and Smadel have obtained the same picture with unwashed stored preparations of vaccinia but when these were re washed immediately before use they presented a high degree of regularity of external outline and internal form. The particles are almost rectangular in shape, resembling a brick, and contain five areas of condensation, the central one being slightly larger than the remaining four. Heating for an hour at 56°C., dehydration in a vacuum over P₂O₅ and drying from the frozen state did not appear to alter the internal structure. The various stages of dissolution by alkali treatment, ranging from swelling, blurring of the edges and decreasing density of the substance to complete laking, could be clearly seen. After exposure to hyperimmune vaccinia rabbit serum, the re washed particles appeared more dense than usual, no internal structure being visible. This suggests that some of the antibody remained attached to the virus particles. A somewhat similar finding in the case of bacteria indicates that soon more light may be thrown on the reaction between viruses and their antisera. It was not possible to designate the limiting structure which separates the virus from the surrounding medium as a semipermeable membrane. Green and his co-workers only say that the surface of the bodies appeared to be different from the main internal constituents. Ruska does not think that the viruses of variola, rabbit myxoma and ectromelia possess a membrane similar to that of the bacteria. However it seems certain that vaccinia virus has a morphological structure which in many respects approaches that of bacteria and differs from that of the plant viruses. This technique may later reveal such interesting facts as a difference in structure between freshly isolated strains and those long passaged in mammals or attenuated by passage in the developing chick embryo.

First Aid Posts*

(From the *Medical Press and Circular*, Vol. CCVIII, 19th August, 1942, p. 113)

It is a good many months now since we first drew attention to the question of our First Aid Posts in general and of certain special categories of Aid Posts in particular. Shortly after we had done so (though modestly will scarcely permit us to claim that it was a case of *post hoc propter hoc*) it was officially announced that the number of these posts was to be substantially reduced. If memory serves us aright the reduction was to be roughly by one-third, and it was to apply especially to those posts established in or close to casualty hospitals, these, as we ourselves and others had pointed out, and as it would seem to have been tacitly admitted, being largely redundant. The promised reduction was no more than a reasonable concession to common sense, and we looked forward to it as a measure which would release young women for other spheres of activity where they were badly needed, as, for example, nursing.

Since then what has happened? Has the reduction been carried out? We cannot say. So far as we have seen, no statement on the subject has been made to Parliament or issued to the Press. And for obvious reasons one cannot know nowadays what has been happening in distant areas. But when we wrote, we wrote with an eye on a number of posts of which we had first-hand knowledge, and which had amply demonstrated their redundancy. Well, they are still there.

Indeed, like the blackout, the blast walls and all the rest of it, they have merged into the war-time landscape and are rapidly becoming traditional. Soon they will be as hard to uproot as the spreading chestnut tree itself.

Let us refresh our memories on the subject. In a report issued some time ago by the Ministry of Health covering the first nineteen months of war (and covering, be it remembered, the worst period of heavy raiding) it was announced that some 2,000 posts had treated some 68,000 casualties. As we pointed out at the time, this meant that each post had dealt with an average of about 34 casualties during that time. And since each post employs roughly about 20 personnel, this gives a figure of less than two patients per employee over a period of more than a year and a half. Frankly this seems ridiculously wasteful.

To consider for a moment the question of Aid Posts in general. What is their value? Officially it is assumed to be enormous. But is it? We do not know of anybody who has made it his (or her) business to study the matter realistically. We have discussed the matter with all and sundry at every opportunity, and especially with surgeons. Many surgeons condemn them out of hand. But the consensus of reasonable opinion seems to be somewhat as follows. Some fixed posts have done excellent work; many have done none at all. Posts without a doctor on the spot are a menace. Seriously injured persons sent to Aid Posts and detained there for any length of time, whether while waiting for a doctor to arrive or for any other reason, do very badly. The double removal is an unjustifiable strain. Air-raid casualties are extremely deceptive. The prime necessity of any air-raid casualty is that he should come under the most highly skilled observation available as soon as is humanly possible. That means removal to the nearest hospital. Time wasted at an Aid Post may have fatal results.

This does not imply that there is no room in air-raid casualty work for First Aid. On the contrary. But by far the best place for First Aid is *at the site of the incident*. In other words, what we really require are far more mobile posts and far fewer fixed posts. The fixed post, in fact, ought to be reserved for areas where the nearest hospital is a considerable distance away, and then it should be one at which an experienced practitioner would be certain to be present once the alert had sounded.

Some time ago the Minister of Health lamented that the shortage of nurses amounts to a surprising deficit of some 15,000. For three years now we have had approximately 40,000 young women engaged in First Aid work, mostly with nothing to do. And to-day they are no forrader. Had suitable arrangements been made, if only in Posts established on hospital premises, he might have had some promising material to draw on, that is, persons trained not only in First Aid but in the general outlines of nursing as well. Even as it is, it may be worth while suggesting to him that he has a reservoir of woman-power closer at hand than he suspects. In any event, the First Aid position deserves to be realistically and drastically explored.

Use and Abuse of Sulphonamides

(From the *Medical Officer*, Vol. LXIX, 9th January, 1943, p. 10)

THE Minister of Health in a recent speech said the lives saved by sulphapyridine in cerebro-spinal fever and pneumonia in 1939-41 exceeded those which the Axis war machine was able to destroy in the Battle of Egypt. He quoted Dr. W. J. Martin's estimate of 10,000 recoveries from cerebro-spinal and 7,500 from pneumonia which would not have been expected had sulphapyridine not been used. This estimate is conservative, and if we add to it the lives saved in other diseases by all the sulphonamides we may find on balance that the discovery of this class of remedy has done more to save life than the war has done to destroy it. The immense value of these drugs is that

* See Editorial, page 348.

they are potent in some of the commonest serious diseases of mankind and have a wide range of utility; but let us be mindful that their action is specific and that where they are impotent their exhibition is useless, dangerous and expensive.

The indiscriminate use of these drugs by the public is bound to do great harm and unlikely to do any good whatever, so their sale should be prohibited except on medical prescription. Our advocacy for this step, which we admit is a drastic one, is that the supply of the drugs is not equal to the legitimate demand for them, whilst their known value is limited to diseases with a high fatality. They may be of use in some of the minor infections for which persons like to treat themselves without calling in expert advice, but there is no proof that they are, and they are definitely dangerous.

Abuse of the sulphonamides is not limited to the public, for medical practitioners both misuse them and waste them. The known fact that they are dangerous is no let to their use by doctors who must experiment with them, but the scarcity of sulphonamides at the present time should limit their trial to those conditions in which they have proved to be valuable, save in the hands of those who are able to carry out experimental work under controlled conditions. So far they have been proved to be valuable in invasive diseases caused by hæmolytic streptococci, pneumococci, gonococci and meningococci. Whether they are useful in staphylococcal diseases is doubtful, but not unlikely. They have no proved value in toxæmias, such as the usual form of scarlet fever, and are most unlikely to have any. They have so far failed to show any promise in acute rheumatisms, or in any virus disease, but they may have value in some of the bacillary diseases, though we cannot say at present that they have. Unless they are used in accordance with what has been established by experiment they are probably always more dangerous than beneficial. At present they are much used locally for wounds. Here they show great promise, but the results are inconclusive and their use for this purpose calls for much more experiment and trial under conditions where the results can be evaluated. The call on the drugs for this purpose is greater than the supply, so we plead again that for the present they should be proscribed and not prescribed for sicknesses in which there is no experimental support for assured benefit.

Surgery in the Middle East

By E. G. MUIR, M.S., F.R.C.S.

(From the *Lancet*, Vol. I, 2nd January, 1943, p. 1)

THE major surgery in the Middle East is as a rule limited to three units—the surgical team or field surgical unit, the casualty clearing station, and the base hospital. The surgical team consists of a surgeon, anaesthetist and a varying number of RAMC personnel, usually drawn, as in the last war, from the base hospitals. They may be used to reinforce a CCS, or may work in the forward area with the light section of a CCS or the main dressing station of a field ambulance. A forward surgical team is likely to be of particular use in mobile and fluid warfare when the absence of a fixed line makes it necessary to keep a CCS a considerable distance behind the forward area.

The equipment carried by a surgical team is designed to allow the team to function on its own for a limited period. Their theatre may be a lean-to tent fixed to the back of a lorry, or a separate theatre tent. Successive advances into Cyrenaica and East Africa resulted in the capture of many Italian hospital tents, and these became popular with surgical teams, either as a theatre or as a ward; double-sided and roofed, and well supplied with windows, they are excellent tents though a little cumbersome to carry. Lighting of the theatre may be by 'Petromax' lamps or from the lorry or truck. The 'Primus' stove is one of the surgical unit's most valuable instruments—as indeed it is with any

unit. The mobility and small size of these field surgical units enable them to be moved nearer the scene of action than a CCS. In Eritrea and Abyssinia the CCS was occasionally as far back as 200 miles from the scene of fighting.

The forward surgical unit shortens the period between the receipt of the wound and its treatment, often considerable in the Western Desert, it provides a surgical opinion in the forward area, and its presence is appreciated by the combatant troops. The surgeon must confine his attention to the very seriously wounded, those with penetrating wounds of the abdomen, sucking wounds of the chest, severe burns, certain wounds of the head and face and serious limb injuries—in fact, the cases which might not be expected to reach the CCS alive. If he starts to treat others a sudden rush of serious casualties will swamp him. One of the difficulties of such units is that once a serious case has been operated on the patient become immobile for perhaps 48 hours or longer and the mobility of the unit may be impaired. As with other forward units they are exposed to ground strafing by enemy aircraft and more than once they have been taken prisoners.

The surgeon in the CCS of the last war must, I think, have had a happier time than his successor in the Middle East. The necessity to keep the CCS further back has led to some of his surgery being stolen by a field surgical unit, and on at least two occasions when casualties have been plentiful, a base hospital has taken over the duties of a CCS, as in Tobruk and later at Alexandria. For a CCS, too, periods of inactivity with few casualties and little work have been frequent in the Middle East and its situation has made this inactivity worse.

Apart from those which are housed in existing buildings, most of our base hospitals have been created by the Royal Engineers, on desirable desert sites, on fine sandy soil with rail facilities, and I have never ceased to wonder at the short time in which a piece of sandy desert is transformed into a 1,200 bed hospital, partly tented, partly hutted, well equipped, with a good water-supply, roads and electric light. Such a hospital experiences perhaps its only disadvantage when a cold sandstorm rages in January or a hot sandstorm or 'khamsein' in May. Nothing will keep out the sand, and as far as is practical dressings are left untouched and operations postponed. To such hospitals the sick and wounded from the desert arrive by ambulance train, and in spite of a journey of perhaps over 200 miles they have usually arrived in good condition.

GENERAL TREATMENT OF WOUNDS

I have not yet felt justified in practising excision and primary suture of any wound. Clean through-and-through bullet wounds are best left alone, apart possibly from the introduction of some sulphonamide powder and the application of an antiseptic dressing. For larger wounds the term excision is misleading, since the ideal to be aimed at is the removal of necrotic tissue, cleansing and the provision of really good drainage. The use of powdered sulphanilamide or sulphapyridine and a 'Vaseline' pack is almost universal in the Middle East for wounds of any size. The importance of immobilization for soft tissue injuries is well recognized and many flesh wounds of the limbs are treated in plaster. Certainly all serious wounds will have begun a prophylactic course of sulphapyridine or sulphanilamide in the forward area, though by the time they arrive at the base hospital their dosage will often have been erratic. Intravenous sulphanilamide or sulphapyridine solutions are easily obtainable and the blood-transfusion service in the Middle East has deservedly won praise for its work.

The usefulness of skin grafts and burns cannot be overestimated. Units in the Middle East are available for those requiring an extensive or difficult graft, but pinch or Thiersch grafts for wounds of moderate size can effect a saving of weeks in healing time and can be applied in any hospital. In the preparation of the surface for grafting we have found a sulphanilamide spray as valuable as

it was economical in the treatment of other wounds. A very efficient substitute for tulle-gras was obtained by purchasing curtain net of small mesh in Port Said or Cairo.

The provision of Army hospitals in South Africa has rendered it unnecessary to retain in a Middle East hospital a patient who is likely to require several months' hospital treatment, and while the surgeon may sometimes regret that he cannot see the end-result of the case there is never any doubt as to the patient's own feelings when he is told that he is to be evacuated.

In Eritrea and Abyssinia the Italian hand grenade caused a high proportion of our casualties. The particular one in vogue at that time was a small red one with a light metal casing. Their size and weight made them easy to carry and the Italians and their native askaris, crouched behind the rocks on the mountains round Cheren, flung large numbers down on our troops. The noise they made was startling, but the fragments had little penetrating power. They caused many casualties with multiple small wounds; direct hits were more unpleasant, but few were fatal. A great number were left by the retreating Italians, and many natives, unable to overcome their curiosity, lost their fingers and their eyesight in attempts to open them.

Among our casualties in Syria was a very high proportion of bullet wounds. The effect of this was most obvious in the compound fractured femurs of that campaign, for most of them, caused by bullet, had little or no sepsis and united as quickly or even quicker than a simple fracture.

The Western Desert has of course produced casualties of all kinds, but compared with the fighting elsewhere land-mine injuries have been very common, such as bilateral fracture of the os calcis from the blowing up of a truck. It has also furnished a surprisingly high number of accidental burns, some of them very serious, caused by the use of petrol in sand fires, usually for making tea. Though hardly a battle casualty, the desert appears to be a bad place for the patient with piles. Many patients say that they are quite well as long as they are not up 'in the blue'. Once there they become constipated and their symptoms recommence. They attribute this to the diet, which can hardly be varied, to the comparative lack of water, and, for some of them, their inability to take liquid paraffin regularly.

PENETRATING WOUNDS OF THE ABDOMEN

To me one of the greatest disappointments of war surgery has been the lack of success with penetrating wounds of the abdomen. The published records of these wounds in the last war had led me to hope that a survival rate of 40 to 50 per cent might be obtained, and indeed, descriptions of casualties in the Spanish War and more recently in civilian casualties at home show results of that order. From my own limited experience and surgical gossip with colleagues I think that the operative survival

of abdominal wounds in the Middle East would be more than 20 to 30 per cent and probably less. Of my own 17 cases only 5 survived, approximately 30 per cent. Perhaps the best picture I can give of the mortality of these cases is the fact that during one year at a base hospital of 1,200 beds only 7 post-operative cases of penetrating wounds of the abdomen were admitted.

Most of these cases are treated by the field surgical unit; only occasionally does the CCS receive them, and the base hospital only under exceptional circumstances. The earliest abdomen on which I operated was 6½ hours from the receipt of the wound; a young officer with a penetrating wound of the ascending colon, destruction of one testicle and a compound fracture of the tibia. The average time which elapsed before operation was about 14 hours. Lieut.-Colonel Ian Aird, one of my colleagues working in the Western Desert, in 18 cases of abdominal wounds, had only one admitted within 12 hours of wounding and only 7 within 24 hours. In East Africa the delay was largely due to the mountainous and difficult terrain, necessitating a long carry by the stretcher bearers, occasionally up to 7 hours. In the

Western Desert it is partly due to the immobility of transport at night and the scattered nature of the fighting. Peritonitis was present on arrival in about three-quarters of my cases.

Heat was an unpleasant factor in East Africa. A shade temperature of 105°-110°F. was common near Cheren. Ether boiled when the cork was removed from the bottle; gas was not then available and chloroform became a necessary anaesthetic. It is not to be recommended for the shocked abdominal patient in whom the surgeon wants relaxation.

" PENETRATING WOUNDS OF THE CHEST AND SKULL

Special centres for the reception and treatment of chest wounds exist in the Middle East. Their treatment in the forward area, however, devolves on the general surgeon. Some of the sucking wounds are closed by the first medical officer who is able to insert one or two tubes. If left alone, the value of such closures is doubtful, since wounds closed in this necessarily slipshod manner are apt to break down badly when infected; there is something to be said in favour of a temporary pack and delaying any closure of the wound until it can be performed under proper surgical surroundings. In general the tendency of surgeons in the forward area has been to deal conservatively with chest cases and to do little more than close a sucking wound. The after-treatment has been repeated aspiration, with or without air replacement, blood-transfusions according to the patient's haemoglobin level, and sulphapyridine. Most cases seem to have done well on these conservative lines. Even when there is a retained foreign body of some size in the chest no early attempt has as a rule been made in the forward area to remove it. Surgeons feel that to attempt to remove a foreign body by an early thoracotomy in such a setting would be to court disaster.

The majority of penetrating wounds of the skull are admitted to a special centre. The initial treatment will be done elsewhere and useful instructions have been issued to all surgeons emphasizing the important points in the examination and closure of such wounds.

COMPOUND FRACTURES

With few exceptions compound fractures have been treated by wound toilette, removal of dead or devitalized tissue, a sulphonamide vaseline pack and plaster. There is no doubt as to the great value of this treatment both as regards the patient's future and the immediate problem of transportation. The faults of this treatment have arisen from technical errors—a tight plaster, excision of too much skin, failure to remove devitalized muscle, particles of clothing or other foreign matter from the wound, and the excessive removal of bone fragments.

Compound fractures of the humerus have as a rule been treated by plaster with the arm to the side unless the type of fracture indicated an abduction plaster.

Compound fractures of the femur remain one of the most serious casualties. Most of these arrive at a base hospital in a Thomas splint with extension strapping, a wound toilette having been already carried out and a sulphonamide vaseline pack inserted. Whether a compound femur should be treated by a plaster spica remains a matter of debate. My own preference, were I ever to suffer from such an unpleasant injury, would be a really wide excision of the wound so that the bone ends could be seen at the bottom of the sloping sides, ensuring good drainage, a sulphonamide vaseline pack, a Kirschner's wire through the tibial crest with weight extension, and a plaster spica from waist to toes, cut open over the knee. After two to three weeks I should prefer to be treated on a Thomas splint. I believe that plaster and packing for the first two to three weeks effectively seals off the fracture from the tissue planes and greatly reduces the likelihood of gravitation abscesses. Excision of the wound is unnecessary in the case of compound fractured femur with a small entry and exit wound of a bullet and no sign of infection; where there is a small apparently uninfected entry

wound and a larger exit wound, only the larger wound should be excised.

AMPUTATIONS

The sites of election for a lower limb amputation are almost standard but when such an amputation should be performed is more debatable. This question does not arise in civil life since a street accident is admitted to hospital with little delay. In warfare a wound of the lower limb, which by its severity requires amputation, is often 24 hours old before surgery is available. It is infected and any amputation performed in its proximity stands a considerable risk of becoming infected also. If amputation is carried out at the site of election and gross infection ensues, further amputation will subsequently be necessary and the patient has then lost the most favoured site. Up to what period after the receipt of a wound it would be safe to choose the site of election must depend on the surgeon and the wound, but in doubtful cases a guillotine amputation at the site of injury would probably be the safest course.

A true guillotine amputation at the site of election can only be justified if there is no other alternative. These amputations are seldom done; in most of the amputations performed in the forward area flaps of some kind have been fashioned, held together with one or two sutures, perhaps over a sulphonamide vaseline pack or occasionally stitched back. Secondary suture has in many cases produced an excellent stump. Of amputations admitted to a base hospital I have seldom seen an amputation stump of the lower limb heal completely by first intention, and when an attempt has been made in the forward area to obtain this by the insertion of many sutures the results have often been disastrous. The inference to be drawn is that if a wounded limb requiring amputation is more than 12-24 hours old, the site of amputation must be regarded as a potentially and perhaps heavily infected area.

Amputation through the knee-joint may be a life-saving measure, but posterior retraction, with perhaps a visible popliteal artery and vein in the infected granulations, is unpleasant and should be avoided if possible.

BURNS

The treatment of burns was one of the subjects discussed at a surgical conference held in Cairo in the early part of 1941. It was noteworthy for the varied opinions expressed. Tanning methods have produced some excellent results but many failures and when these methods fail it would have been far better for them never to have been tried. They are as a rule unsuitable in the forward area unless optimum facilities are present and adequate time for careful cleansing. The use of tannic-acid jelly as a first-aid dressing is now generally deprecated. Treatment by moist dressings is difficult where long lines of evacuation are present and some form of sulphonamide vaseline dressing has much to commend it.

In my experience, most of the severe and extensive burns received at a base hospital, 2-4 days old, have required treatment afresh. Cleansing under an anaesthetic, a sulphonamide spray, and bandaging with six-inch rolls of vaseline gauze is the treatment I have preferred. The patient is given a course of sulphanilamide by mouth and a plasma drip till the hæmoglobin is reduced to 100 per cent. The highest I have seen was 140 per cent, a finding which was confirmed by the pathologist who pointed out that it was actually higher but that this was the highest level he could record. The patient, a South African with second degree burns of more than a third of his body surface, made a surprising recovery. If pyrexia subsides, and the dressings do not become soaked in pus, they are left till they drop off. When secondary infection is present, the dressings are soaked off in a warm saline bath every 48 hours and reapplied. The greater part of these burns is usually second degree but whole skin destruction often only becomes apparent when sloughing appears. For these areas sulphanilamide powder, tulle-gras and

moist dressings are excellent as a preparation for skin-grafting, but for the earlier and more extensive dressings the wide vaseline gauze roll has the great merit of speed in application. Glycerine and sulphanilamide dressings, and the use of plaster for limb burns have their adherents. Some of the more recent methods of treatment recommended in this country have not been available for the Middle East or have been unsuitable.

TETANUS AND GAS GANGRENE

Few cases of tetanus have occurred in the Middle East, which is in keeping with the experience of surgeons who served there during the last war. I cannot say what part tetanus toxoid has played in this low incidence. I have only had one case—the only occasion on which I have been guilty of associating with an unqualified practitioner.

An Arab of the Arab Legion was wounded by bombing during the Syrian fighting. He was admitted to hospital three days later with a large lacerated wound of the thigh and a compound fractured femur. After the usual treatment of the wound he was put up in a plaster spica. On the 12th day he developed tetanus but recovered after a stormy passage. At one time it was feared that he might lose his leg, and his father asked that he should be allowed to call in an Arab bone-setter. I replied that I should be very pleased to consult with him and a few days later he arrived at the hospital accompanied by all the near—and most of the remote—relatives of the patient. He was an imposing figure, 80 years of age, a huge mountain of a man with a large hooked nose and wrinkled brown face. He was a shepherd from Bethlehem Fields who from the age of 6 had been interested in fractures and had gradually acquired a reputation and a practice among his people. We examined the case together and then, with the aid of an interpreter, discussed the treatment. He told me that the Arab believes that a broken bone will heal in the same number of days as the patient's age and requires splinting and rest for this period. Thus the bone of a man of 40 will take 40 days to unite. The rule broke down in the case of infants and in the presence of an open wound. In his practice he made it a rule never to treat a fracture with an open wound but to wait till the wound had healed before taking over the case. I explained that I was not in the happy position of being able to choose my cases and we parted amicably. The patient kept his leg and eventually obtained union.

True gas gangrene has been uncommon, and though I know of several cases I have only operated on one, an Abyssinian patriot in the army of Ras Sayoum, who sustained a compound fractured femur and on whom I performed an amputation.

MORTALITY

The surgical mortality will necessarily be high in the forward area and low at the base. The deaths which occurred in the surgical division of a 1,200 bed base hospital in the Middle East during twelve months were:—

Appendicitis and its complications ..	2
Tonsillectomy ..	1
Pulmonary embolus ..	2
Cellulitis of face ..	1
Multiple burns and bronchitis ..	1
Compound fractured femur ..	1
Fractured spine and ribs ..	1
Fractured skull ..	1
Shell wound of leg; compound fracture tibia and fibula; gangrene; anuria after blood-transfusion in hospital ..	1
Shell wound; compound fractured humerus; admitted with anuria after blood-transfusion in forward area ..	1
Shell wound; compound fractured femur; duodenal ileus on 48th day ..	1
Shell wound; compound fractured femur; secondary hæmorrhage ..	1

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0.45 gm @	„	1	9	9 „
0.60 gm @	„	1	11	3 „

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Of this total of 14, only the last 4 were in men wounded in battle.

Of the surgeons in the Middle East, many are at that stage in professional life when, but for the war, they would have been about to start a surgical registrarship. Instead they now learn their surgery and gain their experience in a different school. This experience is valuable for all but principally for the specialist in certain subjects. For the general surgeon it cannot take the place of what he has missed.

Dangers of Pentothal Sodium Anæsthesia

By A. R. HUNTER, M.D., F.R.F.P.S., D.A.

(Abstracted from the *Lancet*, Vol. I, 9th January, 1943,
p. 46)

FROM the patient's point of view pentothal sodium is an ideal anaesthetic; induction and recovery are much pleasanter than with inhalation methods and it is generally held that vomiting and chest complications are less common, though Rivett and Quaile (1940) failed to confirm this. All the common pitfalls in its administration are readily enough avoided by the experienced anaesthetist. The drug is easily portable and requires only the simplest of apparatus for its use. The makers recommended that it be used only by an expert anaesthetist who has at hand the means of inflating his patients' lungs with carbon dioxide and oxygen.

The indications and contra-indications for pentothal sodium anæsthesia are as follows :—

1. It should be used for short operations where nitrous oxide is unsuitable or not available. It is almost ideal for reduction of fractures; the initial relaxation is good and the period of sleep which follows allows of the application of a plaster without discomfort to the patient.

2. Combined with nitrous oxide and oxygen it is a good second best to cyclopropane for extra-abdominal operations generally.

3. Its value for intra-abdominal operations is doubtful, since relaxation may be incomplete. The combination of spinal anaesthesia and light pentothal sodium narcosis is well spoken of however.

4. It must not be used as the anæsthetic for incision of cervical cellulitis.

5. It must not be used as the sole anæsthetic where there is any possibility of entry of foreign material into the larynx.

6. It is probably unwise to prolong pentothal sodium anaesthesia without taking special precautions to prevent the anoxæmia.

Sulphonamide Resistance in Gonorrhoea

By J. PETRO, M.B.

(Abstracted from the *Lancet*, Vol. I, 9th January, 1943,
p. 35)

SULPHONAMIDE resistance in gonorrhoea may be of three types—acquired, relative and absolute.

Possible factors governing absolute or relative resistance are considered in the light of observations on 956 cases of male gonorrhœa.

An *in vivo* and *in vitro* investigation of 44 cases of male gonorrhoea shows that 5 resistant and 1 relatively resistant strains of gonococci were responsible for 6 cases which failed to respond to adequate sulphonamide treatment.

Investigation of the female host of one sulphonamide-resistant strain of gonococci supported the view that such a strain can be transmitted from one host to another.

The development of resistant strains is probably favoured by inadequate dosage, haphazard tests of cure and the premature cessation of treatment in defaulters.

Until new compounds effective against sulphonamide-resistant strains are evolved, or means found for

resensitizing these strains, treatment in cases infected with a sulphonamide-resistant organism must be by irrigations or artificial fever.

Lymphopathia Venereum

(From the *British Medical Journal*, Vol. I,
2nd January, 1943, p. 17)

THE diagnosis of this disease, often known in this country as lymphogranuloma inguinale (synonyms—climatic bubo, paradenitis, Nicholas-Favre disease), presents considerable difficulties, because the initial lesion is evanescent and, in fact, usually overlooked. . . .

. . . enitis may be due to a variety of . . .

. . . can be little doubt that lymphopathia venereum is far commoner than has been realized, more especially in tropical and sub-tropical countries and in parts of the U.S.A., where it is particularly frequent among negroes. Hitherto most venereologists have relied on the intracutaneous test of Frei: Frei's antigen, made from human bubo pus, has proved highly specific, but the supply, for obvious reasons, is difficult to obtain and maintain. Recently antigens have been made from the brains of infected mice, but these have not proved entirely satisfactory. More recently still it has been found that the virus of lymphopathia venereum can be grown on the chorio-allantoic membrane of the developing chick embryo, and from this source an antigen known as 'lygranum' has been obtained which is free from many of the objections raised against the other two.

Lygranum is essentially a saline suspension rich in virus elementary bodies prepared from chick embryos; it is freed from most of the tissue constituents by differential centrifugation and is formalinized to inactivate the virus. It can be used either for the skin test or for serum complement fixation. For use in both it is standardized by dilution to a strength which is found to give a positive reaction in known cases of lymphopathia venereum and a negative one in normal persons. Control material is prepared from normal chick embryos. The skin test is performed by injecting 0.1 c.c.m. of lygranum into the skin. Readings are taken at 48 and 72 hours, and, if necessary, again at the end of a week; a positive result is indicated by a papule not less than 7×7 mm., and a negative by one less than 5×5 mm. A papule intermediate between these two is considered doubtfully positive. Shaffer, Rake, and Grace and Axelrod found lygranum to be both highly sensitive and specific for skin tests; it was at least equal to human pus antigen and superior to that prepared from infected mouse-brain.

Results with the three forms of antigen were as follows: In 106 persons diagnosed as having lymphopathia venereum lygranum gave 96 positive, 3 doubtful, and 7 negative results; with mouse-brain antigen there were 78 positive, 9 doubtful, and 19 negative reactions. In 42 of the above cases human pus antigen gave 38 positive, 1 doubtful, and 3 negative reactions. Shaffer and his colleagues also found lygranum to be most satisfactory in the complement-fixation test; in 115 persons diagnosed as having lymphopathia venereum the sera of 113 gave definite positive reactions; the two failures occurred in cases of rectal stricture which were also Frei-negative. The interesting observation is made that skin sensitivity often disappears after sulphanilamide therapy and that apparently the disease is not passed from mother to child *in utero*. Another interesting observation is that in 70 persons, either normal or suffering from diseases other than venereal, positive results were obtained by complement-fixation tests in 6 and negative ones in 64, while of 60 persons suffering from venereal disease 31 gave positive and 29 negative results. From this it is concluded that infection with the virus of lymphopathia venereum is often acquired at the same time as other forms of venereal disease.

There can be little doubt that lygranum possesses many advantages over other forms of antigen for skin

tests. It is both highly sensitive and specific: it is obtainable in bulk and is not dependent on supplies of human pus; moreover, it constitutes an antigen for use in skin and complement-fixation tests more efficient

than any hitherto produced. The intravenous use of chick-embryo antigen is said to give unsatisfactory results as compared with mouse-brain antigen, but few venereologists employ this route.

Reviews

BAILEY'S TEXTBOOK OF HISTOLOGY.—By P. E. Smith, Ph.D., R. L. Carpenter, Ph.D., W. M. Copenhagen, Ph.D., C. M. Goss, M.D., and A. E. Severinghaus, Ph.D. Tenth Edition. 1940. Baillière, Tindall and Cox, London. Pp. xviii plus 764, with 448 illustrations, many coloured. Price, 33s.

In the tenth edition of this useful book two new chapters have been added, one on 'morphogenesis' and the other on the organization of nervous tissues. Both these chapters should be very helpful to students. Another feature of this edition is the inclusion of a short list of references at the end of each chapter.

The first two chapters of the book (running into 60 pages) are devoted to a discussion of the structure and activities of the cell, the first chapter deals with the cell after fixation, and the second with the living cell. The structure of the various tissues is presented in the succeeding chapters; this is followed by a description of the microscopic anatomy of the various organs.

A strong point of the book is that care has been taken to discuss the physiological significance of the structures described; the contributors realize, as they say in the preface, that the structures seen under the microscope assume full meaning only when correlated with function.

The printing and get-up of the book are quite good, and it is copiously illustrated, many of the illustrations being coloured.

D.

ILLUSTRATIONS OF SURGICAL TREATMENT: INSTRUMENTS AND APPLIANCES.—By Erlo L. Farquharson, M.D., F.R.C.S.E., Major, R.A.M.C. Second Edition. 1942. E. and S. Livingston, Edinburgh. Pp. xii plus 392. Illustrated. Price, 25s.; postago, 7d.

During this time of war, few new books on surgical procedures have appeared, and in the production of this volume, the author has made a valuable and timely contribution.

The early part, dealing with infusion and transfusion, gives many useful practical details concerned with these procedures, the importance of which, to-day, both at home and abroad, is very great. The section dealing with spinal injuries and tuberculosis is well conceived and presented, a subject often receiving an all too scant consideration. Most of the rest of the work is concerned with fractures of the bones of the limbs and with modern methods of treatment of these.

It is evident that the writer has put into practice some of the best teachings of Böhler, combined with those of modern English orthopaedists such as Watson Jones, and leavened it with many interesting details bearing the stamp of his own practical ingenuity.

The final section is somewhat novel, and takes the form of an atlas of surgical instruments, the full value of which will be appreciated by students sitting for their final examinations.

In view of its title, the book leaves the reader with a sense of incompleteness, and the addition of further chapters covering other fields, or the adoption of a more orthopaedic designation, would be an advantage.

The volume is faultlessly written, and the many illustrations have reached a perfection not often seen; it may confidently be recommended as a work of considerable value to all those engaged in the mass traumatic surgery of the day.

C. M. S.

DISEASES OF THE EAR, NOSE AND THROAT: PRINCIPLES AND PRACTICE OF OTORHINOLARYNGOLOGY.—By Francis L. Lederer, B.Sc., M.D., F.A.C.S. Third Edition. 1942. F. A. Davis Company, Philadelphia. Pp. xix plus 894. Illustrated with 730 half-tone and line engravings on 463 figures and 18 full-page colour plates. Price, Rs. 60

FRANCIS LEDERER's third edition of his book 'Diseases of the Ear, Nose and Throat' is an improvement upon the earlier two.

The numerous illustrations are well done and the main print is clear and easily read. The book appears to have been designed mainly for teachers, but the material will be useful both to students and young specialists.

Pathology has been given its proper and important place, and in particular tuberculosis of various sites has been dealt with extensively. On the other hand, various surgical procedures entailed in this speciality are given very little space and, in the main, description of them is scanty.

It is a pity that one of the great discoveries of the century, 'the sulphonamides', has not been given more space. To abstain from its early use in mastoiditis or any other disease, because it obscures the classical symptoms, does not appeal to us.

A chapter upon the influence of war on diseases of the ear, nose and throat would have completed a well-written book, that will continue to be a valuable addition to our medical libraries.

J. M.

SYNOPSIS OF OBSTETRICS AND GYNÆCOLOGY.—By A. W. Bourne, M.A., M.B., B.Ch. (Camb.), F.R.C.S. (Eng.), F.R.C.O.G. Eighth Edition. 1941. John Wright and Sons, Limited, Bristol (Stonebridge House). Pp. vii plus 490. Illustrated. Price, 15s.

In the present edition the text has been considerably revised and some parts have been largely re-written. There is a new section on post-natal care. We have no doubt that the book will be helpful to students for revision, and to practitioners as a means of quick reference.

R. N. C.

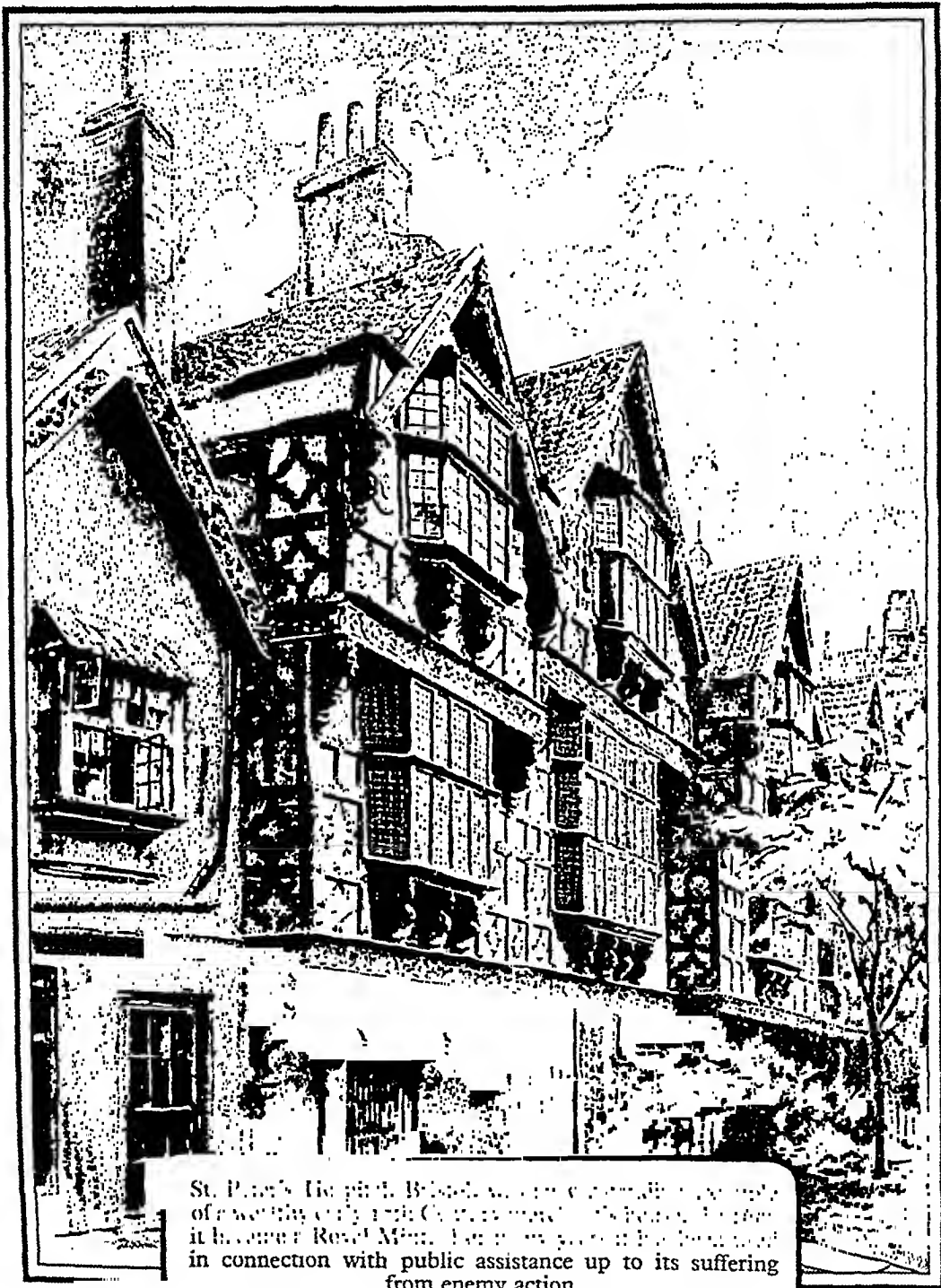
HANDBOOK OF PRACTICAL BACTERIOLOGY: A GUIDE TO BACTERIOLOGICAL LABORATORY WORK.—By T. J. Mackie, M.D., D.P.H., and J. E. McCartney, M.D., D.Sc. Sixth Edition. 1942. E. and S. Livingston, Edinburgh. Pp. xi plus 675. Illustrated. Price, 17s. 6d.; postago, 7d.

THE present edition of this popular book has undergone a considerable amount of revision consequent on the important advances in pathological technique and knowledge since the last edition was published four years ago.

The book is divided into three parts. The first part briefly deals with the biology of micro-organisms and immunity; the second part is devoted to bacteriological technique, providing a very useful guide in practical work; the technical methods are carefully selected. The third part includes a good deal of general information about pathogenic and commensal micro-organisms and their identification; these descriptions are clear and to the point. Virus diseases have been discussed in the last section; this includes amongst others a note

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on infective hepatitis. Finally, an appendix has been added in which some new methods have been described, for instance, the use of *p*-aminobenzoic acid in culture media to facilitate the isolation of organisms even after the patient is given sulphonamide compounds.

The book will continue to serve, as it has done in the past, students, technicians and bacteriologists engaged in routine work.

R. N. C.

Abstracts from Reports

ANNUAL PUBLIC HEALTH AND VACCINATION REPORT OF THE PROVINCE OF ORISSA FOR THE YEAR 1940

THE following is a copy of the government resolution on this report:—

'During the year under report the provincial birth rate was 35.85 per mille against 34.92 in the previous year and the death rate 24.72 per mille against 28.18 in the preceding year. This improvement is mainly attributable to the reduced incidence of the principal epidemics of cholera and malaria and to better agricultural production. The rates of birth and death, however, continued to be higher in the rural than in the urban areas.

No satisfactory progress has yet been made in the matter of ensuring accuracy in the collection and registration of vital statistics; but a definite improvement in the position has been effected in the urban areas as a result of transfer of the responsibility of registration work from the police to most of the municipalities in North Orissa. The question of unifying and improving upon the diverse system of registration of vital statistics is engaging the attention of Government.

The rate of infant mortality during the year under review was lower than in the previous year. Government recognize that the maternity and child-welfare work carried on at different centres is partly responsible for the reduced mortality figures. They trust that the local bodies in the province will realize their responsibility in this important matter of public health and extend the scope of these welfare institutions within their respective jurisdictions and that the public will extend their benevolence to such useful organizations so that at no distant date there will spread over the country a network of maternity and child-welfare centres to ameliorate the conditions of expectant mothers and babies.

Government are constrained to observe that the premier municipality of Cuttack has ceased to contribute its previous annual donation for upkeep of the local maternity centre and they believe that the municipality will reconsider its attitude and revive the help which it used to render before. Government note with pleasure that the centre at Russelkonda competed successfully for the Imperial Baby Week Challenge Shield Competition conducted by the National Baby Welfare Council, London, and was awarded a special certificate for getting the fourth place in the Empire.

Anti-malarial operations subsidized by grants from Government were continued at different centres in the province. Interesting results were obtained from the research carried on the Chilka lake by the fixed unit deputed by the Malaria Institute of India.

The investigation into the life-history of the weeds in the Chilka lake was continued under the supervision of Mr. P. Parija, and the Indian Research Fund Association though unable to pay anything during the year under report agreed to meet the entire expenditure on the investigation in the subsequent year.

During the year under report the incidence of cholera was much less severe than in the preceding year, the number of deaths from this disease being 3,893 against 11,141. The epidemic continues to be a menace as long as the problem of drinking water-supply

is not satisfactorily solved, particularly in the rural areas of the province.

The incidence of smallpox was higher than in the preceding year. Absence of a system of universal compulsory vaccination was no doubt partly responsible for this unsatisfactory situation but the upward tendency of this epidemic was also due to the fact that the year 1941 happened to be the peak year of the usual five-year cycle of this epidemic. With the introduction of the recently sanctioned schemes of compulsory vaccination in the coastal districts of North Orissa and in the union areas of Koraput, the incidence of this epidemic may be expected to diminish gradually in subsequent years. Government have under consideration a proposal of having a unified Vaccination Act for the whole province and when the diverse laws are unified and revaccination made compulsory, a further improvement of the situation can also be anticipated.

Preliminary arrangements for the establishment at Cuttack of a model tuberculosis clinic have been completed, and with the construction of the building which is well in hand the clinic will begin to function under the provincial tuberculosis officer, already appointed, and serve as the foundation of all future developments in the direction of anti-tuberculosis measures in this province.

The anti-leprosy scheme launched by Government has just passed the half-way mark of its tentative experimental period of five years, and is reported to have produced excellent results. The four-fold programme of the campaign, viz, survey, propaganda, isolation and treatment, was vigorously pursued. The foundation of a leper colony in Sambalpur, establishment of more treatment centres and appointment of number of lady leprosy relief assistants were the novel features during the year under report.

The treatment of yaws which is widely prevalent in Agency areas received attention which it deserved. During the year under report a scheme of intensive field investigation into the dietetic and nutritional condition of the people was sanctioned by Government and the work was carried on under the direct supervision of the Assistant Director of Public Health. The investigation has distinct possibilities and with the co-operation of the public in the matter of exposing their dietary habits for analysis valuable data can be available for introducing measures to improve the vitality of the people.

The work in the Provincial Bacteriological Laboratory steadily increased and this necessitated strengthening of the laboratory staff. The Orissa Prevention of Adulteration and Control of Sale of Foods Act, 1938, and the Rules thereunder have been enforced but the local bodies have not yet evinced the required amount of enthusiasm to administer the powers entrusted to them in controlling adulteration of foods. Government cannot too strongly impress upon them the imperative necessity of adequately using the salutary powers vested in them by law and thereby securing better standard of foodstuffs for the people entrusted to their care.'

Correspondence

ECONOMY IN QUININE

SIR,—For those hospitals where quinine is short, and it is necessary to make a pound go as far as possible, the intravenous or intramuscular method will produce the best results with a minimum amount of quinine. With the price of ten-grain quinine bihydrochloride ampoules rising to Re. 1-8 at the chemist's shop it is necessary that something be done. In looking around for a method of converting quinine sulphate into the bihydrochloride, I enquired from Mr. Chouldery at the C. M. A. Hospital Supply Agency, Bombay. He was

able to outline the following method which I wish to describe.

Drugs needed (to convert 60 grammes of quinine sulphate to quinine bihydrochloride):

- (1) 70 per cent sulphuric acid 50 c.cm.
- (2) Saturated solution of sodium carbonate 200 c.cm.
- (3) 10 per cent hydrochloric acid 200 c.cm.
- (4) 2 per cent sodium bicarbonate 20 c.cm.
- (5) Distilled water 1,000 c.cm.

Apparatus needed:

- 4 beakers of 300 to 500 c.cm.
- 1 measuring cylinder of 100 c.cm.
- 2 pipettes of 10 c.cm.
- Filter paper.
- Glass funnel and stand.
- Rubber-capped phials or glass-stoppered bottles sufficient to keep in store about 180 c.cm. of finished product.

Cautions:

- (1) Dilute the sulphuric acid by pouring the acid into the water. Calculate its percentage by weight; if measurement is used there will be a large shrinkage in the volume.
- (2) In neutralizing with concentrated sodium carbonate use the pipette and add only a drop at a time at the beginning, as considerable heat is produced.

Procedure:

- (1) Dissolve 60 gm. of powdered quinine sulphate or bisulphate in the least amount of 70 per cent sulphuric acid that is required to dissolve it. Some heat may be used. Do not worry about foreign matter at this stage.
- (2) Begin neutralization with concentrated sodium carbonate and continue to add from a pipette until all the yellow colour has disappeared and no further bubbles appear.
- (3) Transfer all the precipitate (quinine alkaloid) to a filter funnel and wash thoroughly with distilled water for an hour or two. Sodium sulphate is washed out.
- (4) Transfer all except about 0.3 gm. from the filter paper to a beaker, and redissolve with 10 per cent HCl. It will take about 120 to 150 c.cm. Add slowly and do not use more than is required to dissolve it. When all has been dissolved add the 0.3 gm. left on the filter paper and allow it to stand 3 or 4 hours to see if it all dissolves.
- (5) If it does not entirely dissolve the acidity is satisfactory and the solution is ready for filtration and concentration. One c.cm. of the solution should be made to contain 0.33 gm. of the drug. The required volume is estimated from the amount of drug that was used to start with. For example, if there were 60 gm. of quinine sulphate in the beginning then 60 divided by 0.33 equals 180 times. Place the quinine solution on a water bath and reduce the volume to 180 c.cm.
- (6) If all the alkaloid is dissolved in the latter part of no. 4 procedure it can be suspected that there may be an excess of HCl in solution. To test for an excess of acid take 2 c.cm. of the quinine solution and add 2 per cent sodium bicarbonate (from a burette preferable otherwise from a pipette) a drop at a time keeping count of the number of drops, until crystals just begin to form but no crystals should remain in the solution. (If the solution has no crystals and it has been cooled to room temperature of about 70°F., it is satisfactory.) A proportionate amount of the sodium bicarbonate solution should then be added to the remainder of the quinine solution. It is then ready to be filtered and concentrated as in no. 5.

We have made more than 500 c.cm. of such quinine solution for injection and up to now have had no more complaint than there was after injection of the Indian-made commercial product. These injections should be

given in 200 c.cm. of saline for intravenous use, or intramuscularly in the gluteal muscle on a line midway between the tip of the sacrum and the lateral edge of the ilium.

E. W. WHITCOMB, B.Sc., M.D.

EVANGELICAL HOSPITAL,
TILDA, C. P.
(VIA B. N. RAILWAY, INDIA).

DEATH IN WAR TIME

SIR,—In view of the recent air raids in the south-east of India we feel that the time has arrived when further elucidation on the following points is necessary in the event of an air raid on any town or village:—

1. Diagnosis of death.
2. Identification and disposal of the dead bodies.
3. Question of claim on insurance, property, etc., of an identified and unidentified dead body.
4. Question of missing persons in air raids, the disposal of their insurance, and property.

We therefore draw your attention to an editorial published in the *Journal of the Indian Medical Association* (April 1943), a reprint of which is enclosed for your information and suggestions if any.

K. S. RAY, M.A., B.Sc.,
M.B., Ch.B. (Edin.),
M.L.C. (Bengal),

Editor,
*Journal of the Indian
Medical Association.*

12, HINDUSTHAN BUILDINGS,
CALCUTTA,
21st May, 1943.

[Note.—The copy of the editorial which accompanied this letter is too long to reproduce in full. It discusses the problems of the medical man in war time in areas subject to enemy action and points out the need for medical men to diagnose and certify death. It suggests that the presence of a medical man at a site of an air raid will save lives and also 'unscrupulous persons will not be able to do away with borderline cases'. (Surely this is a rather amazing suggestion.—Editor.) It points out the difficulty of the collection and disposal of dead bodies by the police and emphasizes the need that medical men should be informed what their duties are in the matter and what their remuneration shall be.

The editorial also mentions the matter of certificates; for pensions and compensation for death or injury, and states that the physician should be informed in what form the certificate should be issued. The certificate of identification of the bodies is also discussed and the question is raised as to the death of insured persons and the evidence required by insurance companies. The editorial then quotes at length the rules governing these matters which are in force in England, and points out the need of a similar set of rules in India.—EDITOR, I. M. G.]

Service Notes

APPOINTMENTS AND TRANSFERS

MAJOR (ACTING LIEUTENANT-COLONEL) C. A. BOZMAN is appointed Additional Deputy Director-General, Indian Medical Service (Personnel), with effect from the 1st March, 1943, *vice* Lieutenant-Colonel R. F. D. MacGregor, C.I.E., M.C., I.M.S. (Retd.).

Major W. Scott, Civil Surgeon, Amraoti, has been posted to Hoshangabad with headquarters at Pachmarhi, with effect from the 6th April, 1943.

Major H. A. Ledgard, Legation Surgeon, Kabul, is appointed to officiate as Chief Medical Officer and Civil Surgeon, Delhi, with effect from the 20th April, 1943.

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F.R.C.P., F.R.S.

Formerly Professor of Physiology, University of
London, King's College

and

R. J. S. McDOWALL, M.D., D.Sc., F.R.C.P. (Edin.),
Professor of Physiology, University of London,
King's College.

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Captain A. S. Reilly is appointed to perform the duties of Ex-Officer, Ramgarh Cantt., in addition to his own duties, *vice* Mr. Kohli, granted leave, 22nd April, 1943.

The undermentioned officer of the I.M.S. (E.C.) reverts from I.A.M.C. and is seconded for service in the Royal Indian Navy :—

Captain T. R. Seshadri. Dated 8th April, 1943.

LAND FORCES
(Emergency Commissions)

To be Captains

19th December, 1942

L. M. Mackenzie. D. P. Porter.
A. C. Molden. Dated 25th February, 1943.
S. A. Lateef. Dated 3rd February, 1943.
K. N. L. Iyengar. Dated 5th February, 1943.
R. Bangaru. Dated 15th February, 1943.
A. K. Banerji. Dated 5th March, 1943.
D. Manna. Dated 6th March, 1943.
V. M. Nair. Dated 8th March, 1943.
A. V. Madangopal. Dated 11th March, 1943.
S. N. Sen. Dated 12th March, 1943.
J. C. Sen. Dated 14th March, 1943.
S. K. Kinare. Dated 18th March, 1943.

2nd April, 1943

K. C. Rao. M. M. Ahmad.
L. N. Saxena. C. Koshi.
P. C. Bose. K. S. Iyer.

A. A. Carvalho.

3rd April, 1943

T. P. Row. M. K. R. Panicker.
Md. J. U. Sarkar.

S. G. Yazdani. Dated 5th April, 1943.
B. R. Kashyap. Dated 6th April, 1943.
Clarence Boniface D'Silva. Dated 4th April, 1943.
Gopal Chandra Chatterjee. Dated 5th April, 1943.
Sudhireswar Banerjee. Dated 7th April, 1943.
Kalpathi Gopalakrishna Aiyar Vaidyanathan. Dated 8th April, 1943.

(Women's Branch)—To be Captains

(Miss) Vidya Vati Saberwal. Dated 9th March, 1943.
(Miss) Latif Begum Khan. Dated 20th March, 1943.
(Miss) Mavis Gomez. Dated 23rd March, 1943.
(Mrs.) Greta Barretto (*née* Neri). Dated 25th March, 1943.
(Miss) Alva Adeline Daniell. Dated 27th March, 1942.
(Miss) Hannan Cohen. Dated 14th March, 1943.
(Miss) Mahalakshmi Subbarayalu Naidu. Dated 23rd March, 1943.
(Miss) Leela Nihal Chand. Dated 29th March, 1943.
The undermentioned officers are transferred to the General Service Cadre, with effect from the dates specified.

Captains

B. K. Gupta. Dated 26th January, 1943.
G. K. Chakravarty. Dated 4th March, 1943.
S. Rajan. Dated 21st March, 1943.

Lieutenant

V. Ekambaram. Dated 27th February, 1943.

To be Lieutenants

18th October, 1942

J. F. Cameron. A. W. Howarth.
P. R. W. Leigh.

25th November, 1942

R. M. Craig. A. G. Hick.
A. G. Doughty. G. McCracken.
R. Gardiner. J. M. Murray.

M. W. Grunstein.

F. J. Hopkins-Husson. Dated 6th November, 1942.
H. Din. Dated 28th November, 1942.
S. W. W. Terry. Dated 4th January, 1943.
B. M. Singh. Dated 9th January, 1943.
P. R. Sondhi. Dated 6th February, 1943.
S. A. Hasnain. Dated 18th February, 1943.

H. Chatterjee. Dated 22nd February, 1943.

R. Prasad. Dated 8th March, 1943.

J. H. P. Johnson. Dated 7th December, 1942.

J. D. V. Fitzpatrick. Dated 12th December, 1942.

Denis Patrick D'Vaz. Dated 5th March, 1943.

Duncan Douglas George Passanha. Dated 5th March, 1943.

Philip Jerry Fernandes. Dated 2nd April, 1943.

William Bernard Albert D'Souza. Dated 2nd April, 1943.

Adikesavarao Koka. Dated 3rd April, 1943.

Kamakhyia Prasad Mitra. Dated 6th April, 1943.

Cyril McArthur Hogg. Dated 13th April, 1943.

12th March, 1943, for service in the

Royal Indian Navy

B. N. A. Bootles. P. A. R. Van Ross.

Von C. D. Sausman.

C. A. Hanson. Dated 16th March, 1943.

2nd April, 1943

Dendukuri Anjaneyulu. Amar Nath Lakhota.

Phanindra Chandra Sen. Edmund Basil Naug

Kuruvilla Kurian.

3rd April, 1943

Sibendra Kumar Bhattacharyya.

Kalyan Kumar Dhar.

4th April, 1943

Mohamed Yousuf Siddiqui.

Mohammed Naimuddin Khan Subhani.

The undermentioned officer of the I.M.S. (E.C.) reverts from I.A.M.C. and is seconded for service in the Royal Indian Navy :—

Lieutenant M. A. Chaudhri. Dated 5th April, 1943.

(Within Indian Limits)—To be Captains

Radha Saran Khanna. Dated 4th March, 1943.

B. R. Sharma Rao. Dated 6th March, 1943.

M. A. Narayana Iyengar. Dated 10th March, 1943.

Bindra Ban Gupta. Dated 12th March, 1943.

Narayanassamipillai Sundararajan. Dated 3rd April, 1943.

(Miss) Charlotte De Quadros. Dated 12th March, 1943.

20th March, 1943

(Miss) Kamala Isaac. Dated 4th July, 1942.

(Miss) Pankajam Vedam. Dated 20th December, 1942.

The undermentioned officers of the I.M.S. (E.C.) (Dental) are seconded for service with the I.A.D.C.

INDIAN LAND FORCES

(Emergency Commissions—Dental Branch)

Captain M. Ahmad. Dated 3rd April, 1943.

Captain R. Pratab. Dated 3rd April, 1943.

PROMOTIONS

Majors to be Lieutenant-Colonels

R. A. Wesson. Dated 30th April, 1943.

M. S. Gupta. Dated 2nd May, 1943.

The undermentioned officers are confirmed in their rank with effect from the dates specified :—

Captains

B. K. Gupta. Dated 5th September, 1942.

7th August, 1942

N. N. Singh. A. Sen Gupta.

S. R. Row.

S. V. Krishnayya. Dated 9th August, 1942.

B. D. Mistry. Dated 15th August, 1942.

4th September, 1942

C. A. Rodrigues. A. C. Sood.

T. A. A. Ananthakrishnan. W. J. C. Rebello.

T. R. Krishnamurthy.

5th September, 1942

S. S. Hazra.

S. C. Roy.

C. R. Varkkey.

V. V. Pradhan. Dated 6th September, 1942.

K. N. Raman. Dated 7th September, 1942.

Lieutenants

J. Sanghavi. Dated 4th September, 1942.
D. P. Lahiry. Dated 5th September, 1942.

INDIAN LAND FORCES

*(Emergency Commissions)**Lieutenants to be Captains*

Jogindar Singh Garewal. Dated 19th October, 1942.
S. M. Ghosh. Dated 1st December, 1942.

5th March, 1943

Hassan Din. Rustam Ali Nabi.
P. Chandra. Dated 10th December, 1942.
J. N. Dutt. Dated 22nd February, 1943.

17th March, 1943

N. A. Durham. H. N. Sadhu.
V. Krishnamachary. Dated 19th March, 1943.
27th March, 1943

R. Kumar. A. Rashid.
A. D. Papneja.

31st March, 1943

D. Ramanath. P. K. Mookherjee.
J. I. Rebello. Dated 2nd April, 1943.
M. Anantasayanam. Dated 3rd April, 1943.

11th April, 1943

S. Dass. M. Jamaludin.

12th April, 1943

C. T. Ramachandran. S. Parthasarathy.
13th April, 1943

S. B. H. Gardezi. H. S. Jawanda.
R. N. Chopra. M. Iqbal.
G. G. Prabhu. Dated 14th April, 1943.
S. K. Muhury. Dated 15th April, 1943.
A. J. Vedanayagam. Dated 17th April, 1943.

20th April, 1943

M. Y. Siddiqi. M. N. K. Subhani.
25th April, 1943

S. A. Narayanan. G. Mandal.

26th April, 1943

Z. H. Syed. K. S. Radhawa.
R. Singh.

H. Chatterjee. Dated 28th April, 1943.

(Within Indian Limits)

D. P. Lahiry. Dated 16th January, 1943
J. Sanghavi. Dated 1st April, 1943.
R. R. Dhurjaty. Dated 4th May, 1943.
K. S. Rao. 4th May, 1943.

(Women's Branch)

G. R. Baji. Dated 20th January, 1943.
(Miss) H. K. Nanjamma. Dated 21st March, 1943.
(Miss) C. DeQuadros. Dated 12th April, 1943.

(Dental Branch)—Lieutenants to be Captains

O. C. Verman. Dated 5th March, 1943.
S. Bratt. Dated 6th March, 1943.
H. J. Kundanani. Dated 7th March, 1943.
S. K. Gupta. Dated 8th March, 1943.
C. M. Rego. Dated 9th March, 1943.
H. J. Lobo. Dated 10th March, 1943.
G. L. Narula. Dated 20th March, 1943.

(Dental Branch)

The undermentioned Lieutenants are confirmed in their rank with effect from the dates specified :—

5th May, 1942

G. Mathias. N. R. Vazifdar.
L. R. Bhalla. S. M. Nicholson.
M. D. Mehra.

6th May, 1942

H. D. Gupta. K. C. De.
H. C. Aurora. Dated 7th May, 1942.

5th June, 1942

R. M. Narevala. R. P. Lahiri.
N. S. Sand. E. E. D. Morris.
E. D'Souza.

10th July, 1942
S. D. Gokhale. K. L. Saini.
P. C. Chona.

11th July, 1942
J. Patel. D. V. J. M. Rao.

13th July, 1942
H. N. Bose. O. P. Bhatia.

7th August, 1942
N. G. Nagarkar. E. D. Kavina.
R. C. Kishinchand Kaye. B. N. Ambike.
J. B. Nanda. A. K. Sen.

A. J. P. Oliver. Dated 8th August, 1942.

4th September, 1942
A. B. Marwaha. M. N. Phadke.
M. M. N. Khosla. R. V. Bhagwat.
A. Prakash. N. Pinto.

A. K. Nandy. Dated 5th September, 1942.
M. A. G. Mian. Dated 6th September, 1942.

2nd October, 1942
K. Singh. K. C. Chatterjee.

RETIREMENTS

Lieutenant-Colonel Jamal-ud-Din. Dated 30th April, 1943.

Lieutenant-Colonel E. R. Daboo, M.C. Dated 9th May, 1943.

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Original Articles

'BENGAL SPLENOMEGALY'

(A STUDY OF 50 CASES WITH A DISCUSSION OF AETIOLOGY)

By P. C. SEN GUPTA, M.B. (Cal.)

Officer-in-Charge, Kala-azar Research Department,
Calcutta School of Tropical Medicine

IN hospital practice in south-west Bengal, one encounters a group of cases characterized by massive enlargement of the spleen often associated with hepatic enlargement, not caused by kala-azar, by blood diseases such as myeloid leukæmia, Gaucher's disease, etc., by neoplasm or by infective suppuration such as amæbic or septic abscess. De (1932, 1938) and De and Tribedi (1939), after extensive histopathological and clinical studies, came to the conclusion that this group of cases represented a condition which was different from malaria and from kala-azar, and that the histological picture was suggestive of the action for a long period of an unknown infective element of low virulence. For want of a better term they called these cases 'Bengal Splenomegaly'.

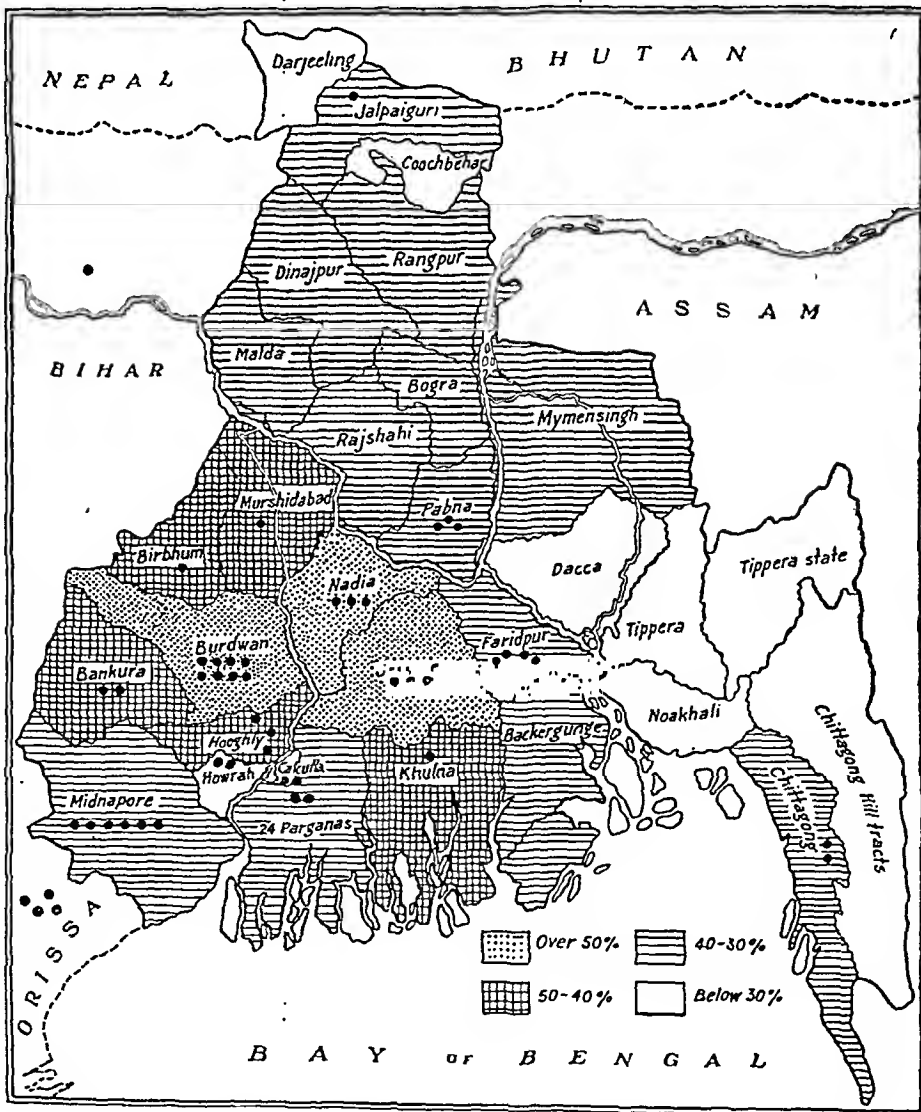
In the School of Tropical Medicine, Calcutta, the cases showing enlargement of the spleen and liver are usually referred to the kala-azar clinic, where they are examined for the presence of leishmanial infection. During the years 1940-42, hæmatological investigations were carried out in a series of 50 cases showing splenomegaly not caused by kala-azar or malaria, and the relevant clinical data regarding these cases were also recorded. Kala-azar was excluded in these cases by the aldehyde test, and also if necessary by sternal or splenic puncture. The patients were usually referred to the kala-azar clinic only after their blood smear had been examined and found negative for malaria, and after they had failed to improve with quinine or einchina febrifuge.

The hæmatological studies included the following

procedures: hæmoglobin estimation; red cell and reticuloocyte counts; estimations of cell volume, mean corpuscular volume, mean corpuscular hæmoglobin, mean corpuscular hæmoglobin concentration; determination of mean red cell diameters and Price-Jones' curve (in some cases); total and differential white cell counts; the van den Bergh test for bilirubinæmia; tests for fragility in hypotonic saline; and the erythrocyte sedimentation test by Wintrobe's method. Standard methods as described in *Hæmatological Technique* (Napier and Das Gupta, 1941) were used.

A brief analysis of epidemiological data and clinical features

The map shows the different parts of the country from which the patients came. It will be noticed that the greatest number of patients came from the districts of south-west and west Bengal. A few patients only came from the adjacent areas in the provinces of Bihar and Orissa.



Malaria distribution in Bengal in relation to splenomegaly.

The figures quoted are based on Bengal Government returns for dispensary attendances.

Each dot represents one case of splenomegaly seen in Calcutta.

Racially, all the patients were Indians; 40 were males and 10 females.

Age.—Table I gives the age distribution of the group of cases. It will be seen that no case occurred below the age of 10 years. Most of the patients were between 15 and 35 years of age.

TABLE I

Age	Number of cases
Up to 10 years	Nil
11-15	8
16-20	8
21-25	16
26-30	6
31-35	5
36-40	3
Above 40	4
TOTAL ..	50

Duration of illness.—The analysis of the duration of illness before the patients came under observation is given in table II. The figure given is bound to be approximate in most instances, as the insidious onset of ill health, the slow progress and the slow and gradual splenic enlargement preclude accurate estimation of the actual beginning of illness.

TABLE II

Duration	Number of cases
1 to 6 months ..	8
6 months to 1 year	13
1 year to 2 years	8
2 years to 3 ..	4
3 " to 4 "	4
4 " to 5 "	4
Over 5 years ..	4
Indefinite ..	5
TOTAL ..	50

Onset.—The onset of illness was insidious in the large majority of cases; in a few cases it was like that of malaria, i.e. with intermittent fever and rigors.

Fever.—All cases except 2 had fever during the course of illness. The fever, usually a low pyrexia, was intermittent in type in 29, low remittent in 3 and of irregular type in 11 cases. Two cases were afebrile throughout the course of illness.

Splenomegaly.—Table III shows the frequency distribution of the size of the spleen in this series of cases. In most cases the spleen was markedly enlarged, i.e. over 5 inches below the tip of the 9th left costal cartilage. The

spleen was firm to the feel in all cases, and the notch could be felt in most cases but not in all.

TABLE III

Enlargement of the spleen in inches below the 9th left costal cartilage	Number of cases
Over 3 to 4 ..	3
" 4 to 5 ..	5
" 5 to 6 ..	10
" 6 to 7 ..	8
" 7 to 8 ..	7
" 8 to 9 ..	12
" 9 to 10 ..	3
" 10 to 11 ..	2
TOTAL ..	50

The liver was enlarged in almost all cases, the enlargement varying; in some the liver was just palpable on inspiration, in others it was up to 3 inches below the costal margin.

There was ascites in 3 cases.

Other features.—The patients usually showed evidence of loss of weight, and some were markedly emaciated. There was slight darkening over the forehead in some patients, but this was entirely unlike the pigmentation seen in the classical case of chronic kala-azar. Slight oedema around the ankles was seen in the cases with marked anaemia, and these cases also showed pulsation of the carotids and often enlargement of the heart, hæmic murmurs being present; a catarrhal condition of the lungs was very frequent.

The principal features of these cases are their marked chronicity, insidious onset, low intermittent or irregular pyrexia, anaemia, loss of weight, slow and progressive enlargement of the spleen which often assumes huge sizes reaching to the pelvis, and enlargement of the liver. A history of hæmorrhages is unusual in the early stages. In the advanced cases, ascites and engorgement of abdominal veins are seen. Bronchitis is seen in a fair number of cases. The only heart changes are attributable to the anaemia; a slight icteric tinge of the conjunctivæ, and even well-marked jaundice is sometimes seen. A history of fever which may be malarial is obtained in some of the cases.

Analysis of the hæmatological data.—Table IV gives a summary of the hæmatological findings in this series of cases and the values of the 'normal' Indian population.

Hæmoglobin.—A comparison of the hæmoglobin values of the male and female patients of this group with the normal values for Indian males and females in Calcutta (Napier and Das Gupta, 1941) shows that the hæmoglobin level of this series of cases is significantly lower than the normal, this fact indicating the presence of a moderate degree of anaemia.

Average volume, hæmoglobin content and hæmoglobin concentration of the red cells.—The values of

TABLE IV

				SUMMARY OF HÆMATOLOGICAL FINDINGS IN 50 CASES OF SPLENOMEGALY		NORMAL INDIANS IN CALCUTTA	
				Males— 40 cases	Females— 10 cases	Males	Females
Hæmoglobin (gm. %)	Mean ± Standard deviation			9.13 ± 2.32	8.009 ± 1.932	14.77 ± 1.36	12.63 ± 1.01
Reticulocytes (% of RBC)	" ± "	"	"	3.11 ± 2.7	3.37 ± 2.39	0.67 ± 0.37	0.37 ± 0.27
Mean corpuscular volume (c.μ).	" ± "	"	"	95.76 ± 11.57	98.94 ± 14.96	90.49 ± 7.90	86.82 ± 7.28
Mean corpuscular hæmoglobin (γγ).	" ± "	"	"	29.62 ± 4.292	29.55 ± 4.21	28.53 ± 2.31	27.42 ± 2.89
Mean corpuscular hæmoglobin concentration (%).	" ± "	"	"	31.16 ± 2.58	30.25 ± 1.596	31.07 ± 1.20	31.57 ± 1.76
Mean corpuscular diameter (μ).	" ± "	"	"	7.423 ± 0.299	7.628 ± 0.267	7.343 ± 0.133	
Mean corpuscular average thickness (μ).	" ± "	"	"	2.13 ± 0.436	1.97 ± 0.227		
Fragility, commencement of lysis (% NaCl).	" ± "	"	"	0.38 ± 0.057	0.40 ± 0.034		
Erythrocyte sedimentation rate (in 1 hr.).	" ± "	"	"	61.46 ± 13.09	69.5 ± 6.05		
White blood cells in thousands per c.mm.	" ± "	"	"	4.81 ± 2.23	4.68 ± 2.84	6.54 ± 1.21	7.16 ± 1.76
Differential leucocyte count :—							
Polymorphonuclears	.. Mean 55.45%						
	Range 28 to 77%						
Lymphocytes	.. Mean 32.70%						
	Range 13 to 56%						
Large mononuclears	.. Mean 7.36%						
	Range 3 to 15%						
Eosinophils	.. Mean 4.0%						
	Range 0 to 20%						
Basophils	.. Mean 0 to 1.5%						
Hyperbilirubinæmia (van den Bergh test).				19 out of 38 cases.	3 out of 9 cases.		

MCV, MCH and MCHC, their means and standard deviations give the range of these findings in this group of cases. Statistical comparison of these values with those for normal Indians shows that the volume, i.e. MCV, is significantly greater than normal, indicating a macrocytic condition. The values of MCH and MCHC are not significantly different, i.e. the cells are orthochromic.

Red cell diameter.—Price-Jones' curves were drawn in 21 out of 40 males and 5 out of 10 females, i.e. approximately half of each group of cases. The mean and standard deviation of mean cell diameters are not significantly different from the normal.

MCAT.—The normal range for the average thickness of the red cells is given as 1.7 to 2.5 (Price-Jones, Vaughan and Goddard, 1935). In this series of cases the thickness lies within this range in all except 3 cases.

Fragility.—In no case was there any increase in fragility evidenced by commencement of hæmolysis at a percentage of NaCl higher than the normal limit of about 0.45 per cent.

Reticulocytes.—A comparison of the mean and the standard deviation of the reticulocyte (per cent of RBC) count with the normal values shows that there is significant reticulocytosis in this series of cases—both in males and females.

The bilirubin content of serum (van den Bergh test).

—The normal maximum for males is regarded as 0.5 mg. per cent and for Indian females 1.0 mg. The males of this series showed values above normal in half the cases, and the females in one-third of the cases in which the test was carried out.

Total and differential leucocyte count.—There was a significant degree of leucopenia in this group of cases, both in males and females. The means and standard

deviations of these groups (males and females) are significantly lower than the values for normal Indian males and females.

The differential count showed a neutropenia with relative increase of lymphocytes in most instances.

The erythrocyte sedimentation rate was higher than normal in all cases.

Summary of hæmatological findings

It will be seen that there is a moderate degree of anæmia, orthochromic and slightly macrocytic in type, with increase of reticulocytes. There is no increase in fragility, and the indications are that there is no marked spherocytosis in most cases. The van den Bergh test shows increased bilirubin content of plasma in about half the cases. A significant degree of leucopenia with relative decrease of neutrophils and increase of lymphocytes is present in an average case.

Discussion

We propose to consider the hæmatological findings first, and then the clinical, epidemiological and other available data in order to discuss the mechanism of production of splenomegaly.

The summary of the analysis of the hæmatological findings shows the changes in the blood picture in this type of cases. The questions that

have to be discussed are (1) What is the cause of the anæmia in these cases? Is the anæmia due to diminished blood formation or to increased blood destruction? (2) What is the mechanism of production of the hæmatological changes seen in this syndrome?

The first part of the question is readily answered by considering the blood changes described above and the pathological picture as described by De and Tribedi. That there is no decrease in red cell formation is evident from the definite reticulocytosis seen in the peripheral blood, and from the other evidence of increased activity of bone marrow seen in the replacement of yellow marrow of the long bones by red formative marrow. A slight degree of defect in the make-up of the red cells is evidenced by the presence of macrocytosis of a slight degree. This is probably nutritional in origin, a restriction of diet due to ill health and/or poverty being the probable cause. The anæmia is thus apparently due to increased blood destruction (there being no history of hæmorrhages in these cases). This view is supported by the histological changes in the spleen, where enormous numbers of large reticulo-endothelial cells with cytoplasm filled with erythrocytes are seen. The anæmia should thus be classified as hæmolytic in type.

The question of the mechanism of production of the blood changes seen in these cases should be discussed by considering the histopathological changes seen in this condition in the light of one's knowledge of physiology of the spleen. According to De and Tribedi, the spleen is enormously increased in size, there is thickening of the capsule, the trabeculæ are numerous and prominent, and the malpighian follicles undergo almost complete atrophy. The splenic sinuses become widely dilated, and are packed with lymphocytes and large phagocytic mono- and multi-nucleated giant cells engulfing an enormous number of red cells and a fair number of leucocytes. Only a very small portion of the actual pulp tissue is thus left. In very advanced cases, both the reticulum and fibrous tissues are considerably increased.

We know that under physiological conditions, the spleen holds a fair quantity of blood in its sinuses, which are lined by modified endothelial cells, and that the sinuses contain, besides blood cells, numerous macrophage cells some of which show phagocytosis of red cells and leucocytes. Both of these types of cells, *viz.*, those lining the sinuses and the macrophages cells, belong to the reticulo-endothelial system. Due to the relative circulatory stasis, under normal conditions these cells are under constant physiological stimulation tending to encourage constant and almost obligatory phagocytosis rather than the facultative phagocytosis sometimes seen as a temporary attribute of ordinary lining endothelium and other connective tissue cells.

Under normal physiological conditions, these cells scavenge the functionally senile and damaged blood cells, particularly red cells, whose

iron content must be conserved for hæmoglobinogenesis. The splenic parenchyma also sequesters blood platelets and granulocytes under normal conditions, and it is well known that the splenic phagocytes may develop a primary destructive selectivity for red cells, blood platelets, or circulating granulocytes with corresponding variation in the symptom-complex, but that the other elements may and usually will be affected to some extent (Doan, 1939).

In the massively enlarged spleen seen in this disease, not only are there immensely larger numbers of blood sinuses and phagocytic reticulo-endothelial cells, but also the circulatory stasis is much more pronounced. The last condition is caused by relative lack of normal rhythmic contractions due to the increase of fibrous supporting tissue and to the relative lack of plain muscular tissue in these spleens. The effect of these factors, *viz.*, intense vascular congestion and circulatory stasis, can only be marked accentuation of what is essentially a physiological process, *i.e.* phagocytic activity of the splenic reticulo-endothelial tissues which in their turn are immensely increased in amount. The marked circulatory stasis and the slightly defective make-up (macrocytic condition) of the red cells probably cause the damaged condition necessary for their phagocytosis. The total effect is the destruction of an abnormally large numbers of red cells, and also to some extent of neutrophils. These facts will explain the mechanism of production of anæmia with granulopenic leucopenia in the cases of splenomegaly under consideration.

We can now discuss the question of the causation of splenomegaly in these cases.

De was of opinion that these cases represented a distinct disease entity caused by an unknown infective element. But in spite of extremely painstaking search he could detect no infecting agent.

A disease of unknown ætiology may easily be wrongly regarded as a manifestation of some known and common infection; for example, kala-azar was wrongly considered as a form of malaria (Rogers, 1897) and as caused by hook-worm infection (Giles, 1892). While we do not ignore the possibility of a hitherto unknown infecting agent being found, we feel tempted to consider the question whether malarial infection, even when it does not cause repeated clinical attacks as in chronic malaria, can possibly lead to splenomegaly of this type.

From the epidemiological data it is evident that these cases come from the intensely malarious districts of Bengal. Most of the cases were between 15 and 35 years of age and there was no patient below the age of 10. (There were very few cases above the age of 40; this is probably because the patients develop splenomegaly at an earlier age period and only a few untreated cases survive middle life.) In these intensely malarious areas, the infants and children are heavily infected with malaria.

and suffer from severe clinical manifestations. If they survive, they develop relative immunity to clinical attacks though they are repeatedly infected by the mosquitoes with the local strains of malaria. The mechanism of development of this immunity is mainly cellular, though there is undoubtedly some humoral factor present, and is dependent on the reticulo-endothelial system (Sinton, 1938). With re-infections especially, there is a marked proliferation of the reticulo-endothelial tissue and acceleration of its functions. Even when as a result of schizogony a number of new parasites are formed, these are prematurely destroyed by the reticulo-endothelium in ever increasing numbers. The effect of this immunity is seen, in the inhabitants of these hyperendemic areas, in the enlargement of the spleen, the largest single reservoir of reticulo-endothelial tissue (high spleen index), and usually in the absence of acute clinical attacks. But we know that the immunity to malaria is labile, and that a lowering of body resistance due to any cause, may lead to acute attacks of fever. As a result of repeated infections with malaria, some of which cause febrile attacks, splenic enlargement of considerable degree may result in some cases. Even at this stage, i.e. when the spleen is considerably enlarged, a balance may be arrived at between the infection and the immunity mechanism, and the patient may be more or less free from acute febrile attacks.

At this stage however the spleen is persistently and considerably enlarged and has already developed a supporting tissue made up mostly of fibrous elements. Due to the consequent relative lack of rhythmic contractions, intense vascular congestion and circulatory stasis are constantly present. The factors—circulatory stasis and immensely increased reticulo-endothelial 'bed' in the spleen—can only lead to obligatory phagocytosis of more red cells by the splenic reticulo-endothelial cells. There is thus demand to increased work. (Besides this there is already a constant demand on the reticulo-endothelial system to combat the repeated infections with malaria in these highly endemic areas.) This leads to work hyperplasia of the reticulo-endothelial tissue. Persistent hyperplasia requires the development of more fibrous supporting tissue and this leads to further stasis; thus a vicious circle is established. The spleen progressively enlarges reaching an enormous size. The patient only occasionally suffers from febrile malarial attacks; the parasites that are introduced into the body are more often than not disposed of by the markedly hyperplastic reticulo-endothelial system.

The other alternative hypothesis as to the mechanism of development of splenomegaly of this type, is based upon the fact that in specific hypersensitiveness to bacterial infection there is an accelerated or exaggerated reaction to contact with the infecting bacterium or its products. It is possible that in this group of cases, hyper-

sensitiveness of a similar type plays an important rôle. Hypersensitive response to even small infections of malaria in these cases can mean exaggerated proliferation of the reticulo-endothelial tissues, as the body reaction to malarial infection is both hypertrophy of the fixed reticulo-endothelial cells and mobilization in the blood of free reticulo-endothelial cells, the histiocytes (Napier, Krishnan and Lal, 1932). It seems probable that repeated hypersensitive reaction to malaria is likely to cause intense hyperplasia of the reticulo-endothelial tissues, and the spleen, the biggest single reservoir of reticulo-endothelial tissue, will undergo massive enlargement.

If we accept any of the above hypotheses regarding the production of splenomegaly, the explanation of other features is relatively simple. The increased blood destruction is for some time compensated for by increased activity of the bone marrow; yellow marrow of the long bones becomes replaced by red marrow. As long as there is adequate compensation, anæmia is prevented, but this mechanism eventually fails and the patient develops anæmia. The reticulocytosis shows that the attempt to compensate for the blood loss is still there, but it is unsuccessful in keeping pace with the destruction of red cells in the spleen; the mechanism of the latter has already been discussed. Other pathological changes that take place progressively in the spleen and elsewhere have been described in full detail by De and Tribedi; hence it is needless to repeat them here.

Acknowledgment

The investigation was undertaken with the encouragement of Dr. L. E. Napier, and it was planned to publish the results of the work jointly, but this has not been possible owing to Dr. Napier's departure from India. The views expressed are those of the author.

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ANÆSTHESIA IN DISTRICT HOSPITALS

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FOR a long time now I have noticed correspondence in the *British Medical Journal* under the heading 'Complacency in Anæsthesia'.

In England there is a fairly wide choice of anæsthetics, from gas and oxygen, its combinations with ether cyclopropane, ether and chloroform alone or mixed, to all the varieties of local, regional, and spinal anæsthesia, intravenous, tracheal, rectal and so on. In England, again, most serious surgery is done by a team, and an anæsthetic specialist is part of that team. He, to a great extent, shoulders the responsibility and anxiety of anæsthesia. Yet there appears to be but little 'complacency' about anæsthesia in the United Kingdom, although so far advanced over the conditions that obtain in the districts of South India. It would therefore be foolish even to suppose that we in India are complacent about anæsthesia. No, we are far from complacent as every office can show from its files. Anæsthesia in South India outside the city hospitals is one long anxiety, and few escape disaster at some time or other; this undermines confidence, and so the efficiency of the staff, and scares away would-be patients in a curable state—so that one disaster may indirectly cause the loss of more than one life. It is, I believe, rare for the actual surgeon to kill. I personally have not known of a 'fatal mistake' being made, and some districts conduct up to forty thousand surgical procedures a year.

What have the district doctors to choose from?

Chloroform or A.C.E., spinal, local and regional, for ether can scarcely be stocked, let alone used, on account of its volatility.

Intravenous anæsthesia is not suitable for prolonged operations, nor does it give sufficient relaxation. Bromethol and avertin are subject to decomposition and so are avoided in a hot place, especially where there is no trained doctor to administer them. Spinal anæsthesia is suitable for the vast majority of cases and I believe is local for all. But here one comes up against the personality of the patient.

With a strong minded patient or with an ignorant trusting patient one can do anything with novocaine or percaine. But what is one to give to the patient who stoutly refuses any

anæsthetic that permits of consciousness in any form while undergoing operation?

Such a patient is a fearful one, and a fearful patient is just the type to die under chloroform.

Before the last war, Dr. Strickland Goodall acquired an electric cardiograph, and being keen to practise with his new acquisition, he subpoenaed his physiology class for experiment for the formulation of data of normal hearts. I was one of that class, and, having started to take a clinical interest in hearts at so early a period, it was only natural that I should gravitate to my teacher's clinic at the Westmorland Street Heart Hospital.

There, Dr. Goodall once gave an amazing clinic, in which he likened the nervous mechanism of certain peoples' hearts to those of rabbits. He expounded on the action of emotion and told us the story of a buck rabbit which, having been kept in solitary confinement, was loosed into the cage of a rutting doe. It died suddenly, and post-mortem examination showed an acutely dilated heart! I well remember Dr. Goodall saying that if one wished to induce experimental ventricular fibrillation, one could do so by frightening a rabbit (now, I doubt not we should give adrenalin) and by giving it chloroform; death is certain and the electric cardiograph will be that of ventricular fibrillation.

Now this knowledge is hardly calculated to give the physician doomed to surgery confidence in chloroform as an anæsthetic, and confidence in any walk of life is essential, if any degree of success is to be achieved; but chloroform is at the present time, in South India, indispensable.

Recently this hospital has suffered a tragic loss.

The patient was a physically fit man of 45 with a sub-acute surgical condition.

Knowing the truth underlying Dr. Goodall's rabbit experiment, I refused to give chloroform. The night before operation, the patient wandered from room to room asking others what they thought of spinal, and went to sleep on allonal with the firm determination to refuse any anæsthetic other than general.

The morning of the operation, he brought forward all his eloquence in firm refusal of a spinal or local anæsthetic, and won the battle only by the threat of a recrudescence of shell shock suffered in the last war. Faced with this situation and realizing that the patient was not in a position to pick and choose his time, I capitulated, and endeavoured to soothe him with promises of cure under complete anæsthesia.

But in a District Civil Hospital there is no choice of general anæsthesia, and chloroform was used. The surgeon stands by reminding himself that adrenalin, whether injected or poured out by fear, plus chloroform produce ventricular fibrillation: and 75 per cent of his attention is diverted towards the course of anæsthesia.

(Continued from previous page)

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The abdomen is not relaxed, the patient is large and powerful, there are long moments of painful suspense, the anæsthetist nods, the surgeon feels the rigid abdomen, and waits again. There is softening of the rigid abdominal wall and the surgeon makes an incision, the blood looks dark, the surgeon stops—looks—listens—no breathing—no heart beat—all is still. Then all the orders laid down by Hamilton Bailey, which are already framed and suspended in the theatre, are carried out, but there is one point that baffles some of us, and it is that the heart is like a uterus, fairly hard and empty, and massage 'feels' useless, and when it does relax, it is the relaxation of death. So chloroform claims one more victim. The hospital and its staff share the responsibility, the public share the fear, and we go on from year to year, from war to peace and to war again, content to give chloroform to all those patients who are too imaginative for local or spinal, just the type of patient for whom chloroform is the greatest danger.

The present is hardly the time to try and obtain expensive apparatus so urgently required for the defence services. Nor can we expect easy and cheap refills of nitrous oxide, oxygen and carbon dioxide or ether in glass capsules. But the world is alive to the necessity for re-planning for a victorious post-war period, and in India no doubt the medical department and colleges will be eager for improvement. Let us make sure that surgical anæsthesia comes in for more than its share of attention to compensate for the neglect of the past, and that a safe general anæsthetic skilfully administered is placed within the reach of all in the post-war world.

What do we jacks of all trades in the districts know about hearts? Just the bare facts of anatomy, physiology, innervation, and a smattering of embryology, and these bare facts are as follows:—

The heart and vascular system are essential to life; disease of the heart impairs the vascular system, and disease of the vascular system impairs the heart. The heart, like all the other organs, has a one hundred per cent reserve to call upon and so takes a lot of knocking out so long as the innervation remains undamaged. And what an important point this latter is!

Anatomically speaking there are two separate hearts, one to pump blood through the general circulation, and the other to pump blood through the lungs. To economize in space, the two are moulded together.

In the primitive reptilian heart, the primitive cardiac tube is differentiated into four primary chambers in this order: sinus venosus, atrium, ventricle, and conus. These contract consecutively, driving the blood through the skin or gills for oxygenation. Later the conus becomes non-contractile (i.e. the first part of the aorta, or bulbus arteriosus) as it is unnecessary to waste effort.

The lumen of the heart then begins to subdivide longitudinally into right venous and left arterial channels by means of longitudinal ridges and septa; the atrio-ventricular opening becomes divided by the junction across of the endocardial cushions and inter-auricular septum; the inter-ventricular septum then becomes established, and the bulbus cordis (conus) completely divided into pulmonary and carotid channels. An alternative observation is that the heart of vertebrates is formed by the fusion of two symmetrically developing tubes, but in any case the fusion and direction of function is from the bulbar, sinus venosus end, caudally.

Now, it is mechanically obvious to any plumber that a pump must have a certain direction of flow, so he puts in valves to control this. So does nature, but nature does not work by a simple matter of *vis a tergo*, but a matter of co-ordinated muscular contractions, so these muscular contractions must be in a definite order to ensure the onward flow of the blood stream.

To ensure this orderly rotation of contraction and relaxation, heart muscle has evolved a state in which it can be refractory or contractile according to its state of nutrition, for after recent contraction, it must relax and is refractory.

Heart muscle is not like the biceps, just a bundle of separate striated muscle fibres each requiring individual stimulation; its muscle fibres branch, each branch uniting with other branches of adjacent fibres, forming as it were, a syncytium; there is no cell limiting membrane such as one sees in the muscle cells of the biceps, and so stimulation of one cell spreads to all (all or nothing rule of Starling).

That is why the heart responds to a needle stuck into it, when, in desperation, the surgeon drives a needle through the fourth intercostal space to inject the heart. It does not matter much, so far as I can see, what the surgeon injects so long as he sticks the needle into the heart, for if the heart is going to react at all, it does so immediately, and not after the injected drug has had time to work. The needle has stimulated a few fibres and the stimulus spreads in a way that it could never do in the biceps.

About auricular fibrillation one knows quite a lot, for it does not kill and we have time to stop and think; Lewis has described the circus waves, and Samson Wright gives all the details worked out for the benefit of the student.

Now the muscle of the ventricle is exactly the same. It has two kinds of fibres, as has the auricle. There are true heart muscle fibres transversely striated and branched, and junctional tissue fibres longitudinally striated. It is these latter fibres that are linked up with accelerator (sympathetic) and decelerator (vagus, para-sympathetic); it is indeed these latter that are all-important in the order of muscular contraction.

What an important thing is this order of muscular contraction; it is the whole point at issue that I have in mind at the present time. If the order of contraction is orderly, we go on happily, but if it is upset, it is like a rowing boat in which each oarsman dips his oar at a different time, and pulls in a different direction, some 'catching a crab'. Such a boat will not only stop, but will be in imminent danger of capsizing.

In auricular fibrillation, the auricle is useless; its impulses are so frequent and to the ventricle so obviously silly, that the ventricle ignores them, and by virtue of its own *junctional tissue*, functions independently.

But what happens when the ventricle suffers the same misfortune?

The circus movement described by Lewis puts three-quarters of the muscle into spasm, the remaining one-quarter being refractory. The heart ceases to function as a pump, and the circulation stops. Death must result.

Samson Wright on page 439 of the 1940 edition says: 'Ventricular fibrillation' may be produced as follows:—

- (1) } (All experimental and of no interest to
- (2) } the practising doctors.)
- (3) }

(4) When low percentages of chloroform vapour are inhaled, the irritability of the ventricles is enhanced to a precarious degree. Injection of minute doses of adrenalin, stimulation of a sensory nerve (e.g. the skin incision); etc., may precipitate fibrillation of the ventricle.

Sequence of events:—

(1) Ventricular extra-systoles arise in one or many foci.

(2) Rapid, almost regular, small undulations of the ventricles occur.

(3) Fibrillation sets in, and co-ordinated contraction of the heart fibres ceases. The heart dilates and the blood pressure falls to zero. Inspection shows that the ventricles are convulsed by minute quiverings; one area is contracted, and the adjacent one is relaxed, etc. 'Clinically, fibrillation of the ventricles has been recorded in the *dying* heart.'

'The earlier stages (1) and (2) have been recovered from. Ventricular fibrillation is the mechanism of sudden and unexpected death, with loss of pulses, pallor passing to cyanosis, and a few gasping respirations.'

It is the fate of the physician doomed to surgery to know the danger, and to experience this very vivid description of the facts. If most of the heart is quivering, it feels like a uterus; the fact that it is taught that a heart never goes into spasm is poor satisfaction, for the very obvious fact remains that a three-quarter contracted heart can contract but little further, and so cardiac massage, although considered a wonderful procedure, is of but little value in ventricular fibrillation of chloroform origin.

How long are we to be complacent in the use of chloroform?

THE NATURAL HISTORY OF A LARGE CYSTIC TUMOUR OF A LONG BONE

By A. T. ANDREASEN, F.R.C.S.

MAJOR, I.M.S.

In October 1936 I was consulted regarding the painful condition of the thigh of the son of a government servant in the employ of the Military Engineering Service. For over six months the boy had been complaining of increasing pain and difficulty in the right thigh on walking. The father thought that his son had always been weak on the right leg, but that recently the boy had been quite lame, and complained that even walking hurt him. He often cried in bed at night.

Clinical examination of the small boy, aged nearly four years, revealed no abnormality, except that he limped badly to the left to take the weight off the right leg. All movements of the joints of the lower limb were free and painless when carried out slowly and deliberately. If any movement, active or passive, was carried out suddenly, yet well within the limits of its range, pain was caused. The right thigh at the upper limits was warmer than the left at a corresponding level. The skin at the same level presented a few visible veins. There was no redness or oedema. There was no increase in the circumference of the affected limb. Deep pressure applied to the right upper thigh was painful and caused the boy to cry out. No other signs could be elicited, although time was spent searching for rarer diagnostic signs. The urine was normal in every way. Blood counts were normal in all respects. X-ray examination of the two thighs, the pelvis and hips showed a very clearly demarcated cystic expansion of the upper part of the shaft of the right femur. Plate XIX, figure 1, is a print of this skiagram. A diagnosis of solitary bone cyst was made, after screening the other long bones and spine to confirm the absence of any other tumours. The position was explained to the father, who refused operative treatment. He was advised of the possibility that spontaneous fracture might occur. He agreed to allow me to see the child once a year as far as that might be possible, considering the liability of government officers to frequent moves. I was able to see this case again in 1937, and in 1938; then after a gap of two years I came across the child again in 1941, and in 1942. At each examination up to 1938, the clinical condition was almost unchanged, the limp and pain persisting. The skiagrams of these examinations (1937 and 1938) are shown in plate XIX, figures 2 and 3. During this time the father, as is the custom in India, had consulted many other doctors, homeopaths, herbalists, ayurvedics, etc. Most of these had simply looked at the old skiagrams and advised various vitamin preparations together with calcium. One had given a course of calcium and parathyroid—I could not

ascertain the dosages—for four months. The father was sure that these had not produced any appreciable change in the boy's condition during this course of treatment.

In 1941, I found that the general condition had improved vastly. The limp, although still detectable, was not really noticeable until the boy tried to run. After a long day of school and games with other boys, he sometimes had a bad night with the pain, but normally he did not complain. He had grown a good deal and looked stronger. Locally there was still tenderness on very deep pressure on the right upper thigh. In the summer of 1939, one of the numerous doctors consulted had advised a course of ultra-violet therapy. This was carried out. The father thinks that the lessening of the pain dates from this treatment. The course was repeated in the winter of 1939-40. During 1940 the pain was much less and the limp became less marked, only appearing when the boy was tired. Another course of calcium and parathyroid was given in the summer of 1940, lasting three weeks. Just over a year had passed from the finish of treatment until I was able to examine the case again in 1941 (plate XIX, figure 4). The boy now plays all games, and knocks about with the other boys of the town in a normal fashion. He has no limp when running, nor has he recently complained of the leg getting tired and painful after excessive exercise. There is still slight tenderness on deep pressure at the site of the lesion. The x-ray showing the present state of affairs (1942) is plate XIX, figure 5.

The series of x-rays taken at long intervals shows a very interesting story of what may happen to one of these cystic tumours of bone when left to itself without operative interference, and without the complication of a spontaneous fracture occurring. The earliest x-ray shows a multilocular cyst of the top of the shaft of the right femur. The cortex is thinned out and the shaft expanded evenly. The upper and lower limits of the cystic area are well defined. The septa of the loculi are well marked. There is no trabeculation, no periosteal reaction, and no surrounding decalcification. The age of the child and the site of the lesion, together with the above observations, serve to postulate a clinical diagnosis of solitary multilocular bone cyst.

How far the calcium, parathyroid, and ultra-violet treatments may have influenced the progress of this particular cyst it is impossible to say. It is, of course, unfortunate for our study of the natural course of this case that these essays in therapeutics should have been made, for they have served to leave a doubt that they may, in some way, have influenced the progress of the cyst; it cannot be said with certainty that the outcome of the case would have been the same without them. That some change was effected is suggested by the fact that after the first irradiation with ultra-violet rays, the pain is stated by the parent to have

been considerably relieved. Whether the bone was affected directly or indirectly by the radiation, is mere speculation; it is not impossible that one of a number of consecutive attempts at treatment coincided with natural changes in the cyst, since the age of the child at this time was about seven years, and he might thus have been in one of the normal 'springing up' phases of child growth (H. A. Harris, 'Bone Growth in Health and Disease').

The case suggests that it might be reasonable to be less pessimistic as to the outcome of such cases where operative treatment is refused. A study of more cases of this nature observed from the early days when the condition is first noticed, and throughout life, together with a study of blood chemistry, x-rays, and, if possible, in the absence of any treatment, would without doubt add to our knowledge of these mysterious bone cysts. (It would however be very difficult to persuade any sensible parent who was aware of the diagnosis to leave his child without any form of therapy.) The warning that spontaneous fracture may occur must always be given, but it seems doubtful whether it is justifiable to plead for operative interference with a view to avoiding such an occurrence.

The case suggests that there may be some cases of such cysts which are never diagnosed and which undergo natural recovery without fracture or interference. A more conservative attitude would therefore appear to be possible. A very painful limp could be treated easily by a caliper or other supporting apparatus without the discomfort and prolonged after-treatment required by operative measures.

Disappearance of bone cysts might well be looked for at the growth periods of human development. Those cysts persisting beyond the times of closure of the latest epiphyses would perhaps be likely to require more active treatment.

The problem of what provides the stimulus for the remodelling to normal of a cystic bone, and of how we can imitate such a stimulus, remains to be solved. The stimuli of opening, scraping and crushing the wall of such a cyst appear to me to be too gross. No harm could come, and great benefit might be reaped, by the trial of simpler but less mutilating methods.

A study of the skiagrams shows that the bone changes are progressive. The story of sudden clinical improvement would suggest that we might expect some dramatic change in the bone condition. This is not seen. But the steady decrease in the cystic appearance is seen to take place from the upper and lower poles, less from the central walls. The hard clear demarcation of the upper and lower poles disappears, to be replaced by bone of normal texture. This fact suggests that in cysts which tended to persist unchanged, remodelling might be stimulated by operative breaking down of the upper and lower poles, e.g. by boring with a fine

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A CASE OF CHRONIC STAPHYLOCOCCAL ABSCESS OF THE PATELLA

By A. T. ANDREASEN, F.R.C.S.

MAJOR, I.M.S.

The clinical picture

THE patient, a young recruit in a Gurkha Regiment, was admitted into hospital complaining of a painful knee, of three weeks' duration. He had had a week's out-patient treatment.

The history was that a year ago, before joining the army, he had fallen down a hillside close to his home in Nepal, and had injured his knee. The knee was badly abraded, and swelled so much that he was unable to use it for about a month. Gradually the swelling subsided and he commenced to get about again. For some time, the knee swelled after walking for any length of time. This, too, had ceased to occur for perhaps three months before coming for recruitment. He passed the medical examination, and was duly sent to a depot for training, where he had been eleven weeks doing all that was demanded of him, when he noticed that after strenuous exercise the knee became slightly swollen and stiff. This, however, passed off during the nights, and he was quite ready to carry out his duties in the mornings again. For two weeks this swelling and stiffness did not so inconvenience him that he could not do duty, but during this last week the knee has tended to remain swollen in spite of the night's rest, and there has appeared a definitely painful spot over the point of the knee cap. This point he defines very clearly.

The out-patient medical officer reported that, when first seen, the right knee was diffusely swollen, that active movements were restricted but not painful, and that passive movements were only restricted by the swelling present. The swelling itself was mainly in the position of the anterior compartments of the joint and the supra-patellar pouch. It had the tense elastic feel of a sac containing its full capacity of fluid. No point of tenderness could be located except over the centre of the patella, and this was not very marked. As no improvement

(Continued from previous page)

Kirschner wire after the technique employed by Böhler for certain ununited fractures.

Pain evidently improves, and the protective limp with it, when the bony remodelling has reached a stage where the normal stresses and strains can be taken by the bone without any shear or bend occurring. The pain mechanism is obscure, but must be explained by any adequate theory of pain mechanism.

I am indebted to Major J. Boal, R.A.M.C., and to Major Ali, A.B.R.O., for their helpful discussions of the skiagrams, and to Lieut.-Colonel J. Shepherd, I.M.S., for kindly reviewing the case with me.

occurred after one week's rest, the man had been sent for admission to the surgical wards.

On admission, the condition of the knee was found to be much as described by the out-patient medical officer, with the addition that there was considerable wasting of the right quadriceps, that the knee was held in slight flexion, that the swelling was hot, and that small blue veins were visible through the skin over the swelling. No redness was present, but a small patch of œdema covered the quite circumscribed area of tenderness on the centre point of the patella. The patient had a temperature of 99.8° in the evening of the day of admission. (There was a daily rise of temperature to 100° in the evening, up to, but not after, the day of operation.)

General examination revealed a well-built young man of Gurkha race, aged about 17. The only other abnormality found was a pair of enlarged tonsils. They showed some scarring, and a small bead of pus was expressed from the left one.

Auxiliary examinations

The urine contained no abnormal substance. A total white blood cell count was mildly increased, i.e. 9,000. A differential count demonstrated the increase to be due to a polymorphonuclear leucocytosis. Fluid withdrawn from the affected joint by puncture with an exploring needle and syringe was opaque and yellow, but flowed easily through the needle. Microscopic examination showed large numbers of polymorphonuclear leucocytes, both alive and dead, but no organisms of any kind. Cultures remained sterile. Meantime an x-ray examination of the joint had been made. The lateral picture, reproduced here (*see figure on plate XX*), shows a fairly well-defined cavity in the centre of the patella, which appears to contain some debris. There is some sclerosis around the cavity. The swelling of the knee due to fluid in the synovial sac is also clearly seen in the film.

Diagnosis

From the data collected, including the laboratory reports, a diagnosis of chronic non-tuberculous bone abscess was made.

Treatment

Since the joint was not infected, it was decided to open the bone abscess through a strictly limited incision over the patella. The operation was performed under general anaesthesia (chloroform followed by ether), and with the aid of a tourniquet. The joint contents were completely aspirated before the incision was made. A small curved incision was made on the lateral side of the œdematous area on the patella, and enclosing this area within its concavity. The tissues were raised down to bone, and then lifted off the front of the bone. A soft area of bone, discoloured pinkish grey,

PLATE XIX

THE NATURAL HISTORY OF A LARGE CYSTIC TUMOUR OF A LONG BONE : A. T. ANDREASEN



Fig. 1.—Shaft of the right femur.



Figs. 2 and 3.—Skiagrams taken in 1937 and 1938. No change.



Fig. 4.—Skiagram taken in 1940. Improvement.



Fig. 5.—Skiagram taken in 1942. Marked improvement.

PLATE XX
A CASE OF CHRONIC STAPHYLOCOCCAL ABSCESS OF THE PATELLA :
A. T. ANDREASEN (PAGE 380)



Figure showing a well-defined cavity in the centre of the patella, which appears to contain some debris; there is some sclerosis around the cavity.

A CASE OF HÆMOTHORAX : B. L. CHOPRA (M. H. P. PAGE 393)



Fig. 1.—Showing pleural effusion of the left side with displacement of the heart to the right.

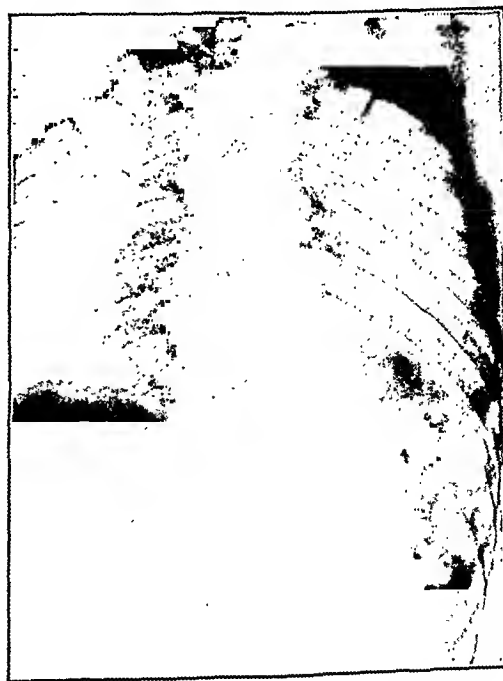


Fig. 2.—Showing fracture of the ninth rib of the left side.

was thus uncovered, almost exactly in the centre of the patella. A gouge was employed to cut out the abscess cavity complete without opening it. This manœuvre allowed the surface of the patella left to have a very shallow saucer shape, thus leaving no corners or dead space. The soft tissues fell into place neatly; two loose through and through sutures held the flap in place and a small strip of gauze at the lower end of the wound provided for drainage.

Examination of specimen

The specimen was sent to the pathological laboratory, where, with aseptic precautions, the abscess cavity was opened and cultures were prepared from the contents. A small amount of bone debris lay in the centre of the cavity, surrounded by faintly yellow, thick pus. Direct smears stained with Gram's iodine showed small clumps of gram-positive cocci, most staining deeply, but a few not so well. Cultures identified the organism as the *Staphylococcus aureus*.

Progress

The patient made an uneventful recovery. Active quadriceps contractions were begun on the fourth post-operative day. Active exercise for the knee joint and its surrounding muscles was begun on the eighth day, two days after the stitches were removed. The joint swelled no more after emptying at the time of operation. Now six months after the operation, and following removal of the tonsils one month ago, the patient is a fit and useful soldier, carrying out all the duties required of him.

Discussion

The long interval between what was probably the initiating and localizing injury, and the final flare up under the stress of military training, is interesting, particularly because during the interval the man must have done a great deal of walking and climbing in his daily life, his home being in the mountainous country of Nepal. It might be surmised that, during this quiescent interval, the organism lay dormant, or that its virulence waned. The regular stress of military life with little opportunity for a rest was probably the exciting factor in causing the final flare up of the dormant focus. At home he could rest when he wished. If it was the virulence of the organism which had waned, then some unknown conditions must be invoked to account for the rise in pathogenicity of the organism at a time when the man had been placed under better conditions than he had ever known in his life before.

The other points of interest are the location of the abscess and the accompaniment of chronic infection of the tonsils. Unfortunately cultures from the tonsils produced such a variety of organisms that it was not possible to offer any reasonable speculation on the possible connection

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ALKALINE PHOSPHATASE IN BONE TUMOURS

By R. G. CHITRE, M.Sc., Ph.D.

(From the Department of Laboratories, Tata Memorial Hospital for the Treatment of Cancer and Allied Diseases, Bombay)

MANY tissues contain enzymes which will hydrolyse the organic phosphorus compounds to give free phosphoric acid. These enzymes are known as phosphatases. Some of these phosphatases are most active in an alkaline medium and the others in an acid medium. The phosphatase of bone (Yamane, 1931), bile (King and Armstrong, 1934) and white blood cells (Roche, 1931) are alkaline phosphatases, while those of liver, kidney (Bamann, Riedel and Diederichs, 1934), prostate (Gutman and Gutman, 1938) and red blood cells (Roche and Latreille, 1934) are acid phosphatases. The phosphatases from the normal lymph nodes, Hodgkin's nodes and lympho-sarcoma, contain both acid and alkaline phosphatases (Woodard and Craver, 1940). Both acid and alkaline phosphatases are normally present in the blood serum. The major portion of the alkaline phosphatase is obtained from bone.

Since Robinson in 1923 first indicated the important rôle of phosphatase in the process of ossification, much effort has been expended in defining the occurrence and characteristics of this enzyme. Kay in 1929 and Roberts in 1930 reported the quantitative phosphatase determinations on the blood of patients with diseases of bone, and introduced this procedure into the clinical studies of bone lesions. Their reports showed that the activity was highest in Paget's disease of bone, a finding which was later confirmed by Gutman and Gutman (1935) and by Williams and Watson (1941).

These and other findings established that, except in cases with jaundice, the serum alkaline phosphatase is increased whenever there is a tendency for the body to form a new bone, or an attempt to do so. Thus, it is high in normal children because the bone is growing. It is very high in rickets because the bones are attempting to grow but are prevented from doing so by some factor or factors which are responsible for the faulty calcium and phosphorus metabolism

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between the two foci of sepsis. The location in the centre of the patella is curious. The history of overlying abrasions may account for the site; infection of a small but severely traumatized portion of bone might occur from a directly overlying septic ulcer. The occurrence of a chronic non-tubercular bone abscess in the patella must be extremely rare; no instance of such an abscess has ever come to my notice before, during ten years of active surgery in a country where cases of bone infection are a daily occurrence.

in that disease. It is high in hyper-parathyroidism, and the excess production of phosphatase probably indicates the defence reaction on the part of bones against the osteolytic process, which is stimulated by parathyroid hormone. The serum phosphatase is usually high in cases with primary or metastatic bone tumours. Franseen and Simmons (1935) and Franseen, Simmons and MacLean (1939) discussed the serum alkaline phosphatase content in a large series of cases of different types of bone tumours, and were impressed with the value of studying this matter in differentiating tumours and detecting the onset of metastases in bones.

Although high values were not entirely confined to any one type of tumour, the highest figures were seen in osteogenic sarcoma, and a rough parallelism was traced between the amount of ossification (judged either by radiography or by morbid anatomy) and the level of serum phosphatase. Unexpectedly high figures were found in cases of bone metastases. Woodard, Tombly and Coley (1936), Gutman, Tyson and Gutman (1936), Woodard and Higinbotham (1937), Roe and Whitmore (1938) and Cade, MacLagan and Townsend (1940) have more or less supported these findings.

At this hospital during the last 1½ years, it has been possible to study the phosphatase content of the serum in the blood of patients with bone tumours, and it was thought worth while to scrutinize the data in the light of the above findings, and to prepare a note preliminary to a more detailed investigation contemplated in future.

Results

The phosphatase determinations were done in the serum of patients by the method of Bodansky modified by Giri and Shourie (1939). The interpretations of results were done on the assumption that the normal value of serum phosphatase in children ranges from 3.1 to 13.1 Bodansky units and in adults from 1.5 to 4. Any value above 3.5 units (in adults) was interpreted as indicating a tendency towards an increase. In table I are shown the results in 18 cases of bone tumour, and in table II are shown the values of serum phosphatase in tumours showing secondary bone metastases in radiograms.

Discussion

1. *Benign giant cell tumours.*—From table I it can be seen that the serum phosphatase

TABLE I
Bone tumours

Serial number	Sex	Age	Approximate area invaded by tumour, cm. ²	X-ray gradation*	Duration	BLOOD STUDIES					
						Calcium mg. %		Phosphorus mg. %		Phosphatase Bodansky units	
						Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
(a) Benign giant cell tumours											
1	M.	23	..	—	2 years	8.6	..	4.1	3.6	4.1	3.1
2	F.	22	13 × 10	—	1 year	9.2	..	4.0	..	3.3	..
3	M.	41	25 × 25	+	8 years	7.0	9.9	4.9	4.7	3.1	2.8
4	M.	9	5 × 5	—	9 months	9.6	..	4.7	..	3.6	..
(b) Ewing's tumours											
5	M.	20	..	+	9 months	9.4	..	4.8	..	3.2	..
6	M.	44	..	—	9 "	11.2	10.7	3.1	4.4	2.9	2.8
7	M.	50	..	+	6 "	10.0	..	3.9	..	4.1	..
8	M.	30	..	—	4 "	10.0	..	6.2	..	3.0	..
9	F.	6	..	—	8 "
10	F.	23	..	—	8 "	9.4	..	5.4	..	4.6	..
(c) Osteogenic sarcoma											
11	F.	10	2.5 × 7.5	+	9 months	12.7	12.5	6.4	5.04	10.3	5.0
12	M.	26	5 × 8	+	5 "	7.6	8.0	4.6	4.7	3.8	3.2
13	M.	20	25 × 25	++	1 year	9.0	..	5.5	..	3.3	..
14	M.	19	..	—	1 "	9.2	..	3.8	..	3.1	..
15	M.	36	..	+++	2 months	9.4	..	4.5	..	3.9	..
16	M.	23	4 × 2	+	4 "	9.6	..	4.1	..	2.5	..
17	M.	34	20 × 14	—	6 years	10.9	..	4.1	..	3.8	..
18	M.	24	7 × 7	+++	9 months	10.4	10.4	4.4	4.4	11.6	3.6
19	M.	15	6 × 9	++	2 "	9.2	10.3	6.8	5.0	5.2	4.2
20	M.	15	10 × 6.5	+++	3 "	10.6	..	6.2	..	33.8	5.8

* — No evidence of new bone formation.

++ Considerable new bone formation.

+ Traces of new bone formation.

+++ Large amount of new bone formation.

TABLE II

Serial number	Age	Sex	Primary	Metastases: (x-ray findings)	Calcium mg. %	Phosphorus mg. %	Phosphatase Bodansky units
21	48	F.	Carcinoma left breast	Metastatic deposits scattered about in pelvic bones.	9.0	4.5	4.7
22	19	M.	Reticulum cell lympho-sarcoma.	Metastases of the ribs	8.0	4.2	11.8
23	66	F.	Carcinoma left breast	Metastatic fracture of the right femur	9.8	4.7	2.5
24	50	F.	" " "	Extensive metastases from the 10th dorsal to 3rd lumbar.	11.2	4.4	6.0
25	52	F.	" " "	12th dorsal, lumbar, pelvis, left femur show extensive metastases.	..	5.0	3.5
26	62	M.	" prostate	Deposits in the lumbar vertebra	11.3	3.5	4.5
27	60	M.	" "	Osteoblastic type of metastases, ribs, spine and pelvis.	11.4	3.8	8.2

did not increase in these cases. These findings are in agreement with those of Franseen and Simmons (*loc. cit.*), and Woodard and Higinbotham (*loc. cit.*).

2. *Ewing's tumour*.—Table I contains the results of blood phosphatase in 6 cases of Ewing's tumour. Like benign giant cell tumour, this group also does not show any notable deviation from the normal values of the serum phosphatase. Some of the authors quoted above (Franseen *et al.*) also found that, although Ewing's tumour is a malignant tumour causing metastases of the bone, the value of serum phosphatase is but rarely increased. This is probably because, in such types of tumours, a mere destructive process is predominant and there is no evidence of any new bone formation.

3. *Osteogenic sarcoma*.—Table I also includes the results of 10 cases of osteogenic sarcoma. The values for serum phosphatase in these cases ranged from 2.5 to 33.8 Bodansky units. In 4 cases (12, 15, 17 and 19) there was a tendency towards a rise and in 3 others (11, 18 and 20) there was a definite increase in serum phosphatase before treatment. In case 11 the value of serum phosphatase (10.3) appears to be within the normal limits for that age, but the very fact that immediately after the operation it came down to 5.0 lends support to the idea that the pre-operation value was increased. It should further be noticed that this low value remained for months until again the case was readmitted for metastases. Before death, when the metastases were detected radiographically, the value was again 9.6 units. In 2 other cases the pre-operative values were much higher than the normal maximum for the age, and came down after surgical treatment.

Unfortunately it was not possible to estimate the serum phosphatase in every case after treatment, but in 5 cases in which such estimations were done, the phosphatase level showed a definite tendency towards a fall. In cases 12 and 19—in spite of little or no rise in the initial values—there was a slight fall after surgical treatment. In cases 11, 18 and 20 the fall was more pronounced. In the remaining 5 cases

the values of serum phosphatase were more or less unchanged. These results do not agree with those of Cade, MacLagan and Townsend (*loc. cit.*) and Franseen *et al.* (*loc. cit.*). In this connection it is, however, interesting to review in short a recent publication by Woodard and Higinbotham (1941). The authors have investigated this problem more exhaustively and their results are interesting.

In 34 cases of osteogenic sarcoma they have found that there were some cases in which both serum and tissue phosphatase values were high. In others the tissue phosphatase was low while the serum phosphatase was unusually high. In still others the tissue phosphatase was high but the value for serum phosphatase was within normal limits. Low values for both serum and tissue phosphatase were also encountered in few cases. In short, the authors found no definite correlation between the level of serum phosphatase and its concentration in the tumour tissue. According to Franseen *et al.* (*loc. cit.*) the level depends primarily upon the product of two factors: (1) the rate of growth or the osteoblastic activity of lesion and (2) the size of lesion. It was therefore thought worth while to correlate the total quantity of the phosphatase in the lesion rather than its concentration. Hence the figures reported by Woodard *et al.* were recalculated by taking the product of the volume of the tissue and its phosphatase concentration. These new values also could not be correlated to the level of serum and tissue phosphatase. The present investigation also showed variable rise in blood phosphatase even though the size of the tumour, the duration of the disease and the osteoblastic activity judged both histologically and radiologically were very similar.

These findings suggest that there is some factor or factors other than those mentioned above which determine the level of serum phosphatase in bone tumours. It is probable that in some tumours, the surrounding media—owing to causes unknown—destroy the enzyme or mechanically prevent it from passing into the blood stream, or the enzyme may be destroyed

in the blood stream itself. A possibility of an enhanced excretion also in some cases cannot be overruled. To elucidate these points a more elaborate investigation is essential.

4. *Carcinoma with secondary metastasis to bone*.—Fransen *et al.* (*loc. cit.*), Woodard *et al.* (*loc. cit.*) and Cade *et al.* (*loc. cit.*) have pointed out that the phosphatase activity in serum serves as a valuable guide in detecting secondary bone metastasis. It had been possible to study 7 such cases, and the results are summarized in table II.

These cases were such that secondary bone involvement was suspected radiographically. Out of 7 cases so studied, the phosphatase activity was increased in 5 while in 2 it was normal. These findings are in agreement with the observations of earlier workers. The fact that the increase in serum phosphatase is not so marked with the secondary bone lesions as with the primary, is explained on the grounds that in the former case the high phosphatase level probably denotes the defence reaction on the part of the bones against the invasion of tumour, and therefore the osteoblastic activity is limited. This can further be seen from table II. The nature of bone metastasis in all cases except in case 27 was not osteoblastic, and therefore very little elevation of the serum phosphatase value was seen. In case 27 in which the osteoblastic activity was more pronounced, the increase in serum phosphatase was more marked.

Summary and conclusions

Four cases of benign giant cell tumour, 6 cases of Ewing's tumour and 10 cases of osteogenic sarcoma were examined for the level of alkaline serum phosphatase in Bodansky units.

Serum phosphatase was not increased in cases of benign giant cell tumour and Ewing's tumour.

Of 10 cases of osteogenic sarcoma, there was a tendency to rise in 2 and a definite increment in 3. In 5 cases the values were within normal limits. In all the cases in which the serum phosphatase was studied before and after operation, there was a fall in phosphatase value after treatment.

These results, in addition to many more in the literature, suggest that the level of serum phosphatase in bone tumours is determined by some factor or factors which are not yet clearly understood. Further work is therefore essential to throw more light on the phenomena.

Of 7 cases of cancer with secondary metastases in bones, there was a rise in serum phosphatase in 5; these findings are in agreement with those of earlier workers.

The author is greatly indebted to his colleagues at the Tata Memorial Hospital for their assistance during this investigation.

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TRANSMISSION OF MALARIA THROUGH TRANSFUSION OF BLOOD

By C. R. DAS GUPTA, M.B., D.T.M. (Cal.)

(From the Department of Haematology, School of Tropical Medicine, Calcutta)

THOUGH the induction of malaria by injection of parasitized blood is not a new idea, and has long been in use in the treatment of cerebro-spinal syphilis, the first authentic report of accidental transmission of malaria through transfusion of blood was probably made by Woolsey in 1911, who reported the transmission of quartan malaria through blood transfusion in a case of pernicious anæmia. Since then, numerous cases have been reported from many countries. Accidental transmission of malaria through intramuscular injection of whole blood was reported amongst others by Wright in 1938, and Nabarro and Edward in 1939, while numerous cases are on record of accidental transmission of malaria in narcotic addicts through the use of hypodermic syringes which are used indiscriminately both for intravenous

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and subcutaneous injections with little or no cleaning.

Transfusion of blood is now a recognized therapeutic measure in the treatment of various diseases, and its use is every day on the increase. With the increased popularity of transfusion, the problem of finding suitable non-malarious donors is also increasing, especially in places such as Calcutta. For, although in Calcutta itself malaria is not highly endemic, primary infection occurring in the city itself is not uncommon. Its inhabitants, however, are more usually infected through short visits to adjacent or remote endemic areas outside the city. In the Civil and Hospital Transfusion Service, Calcutta, blood donors are always selected from strong healthy adults who are free from syphilis and from allergic manifestations of any kind, and they are also supposed to be free from latent or chronic malaria. But it cannot be said with any degree of certainty that latent malaria is totally absent in a donor in the city, and that malaria might not be transmitted through transfusion of blood from such a donor. The following case will show how malaria was transmitted from a donor who was regarded as one of the healthiest donors in the panel :—

Case note

The patient, a female, suffering from myeloid leukaemia had three previous transfusions of blood in the course of a month from donors supplied by the Civil and Hospital Transfusion Service, without any untoward results. The patient had the fourth transfusion on 11th April, 1943, with fresh citrated blood from an apparently healthy donor; there was no reaction. On 16th April, 1943, that is 5 days after transfusion, the patient developed high fever with a rigor. Examination of the blood showed heavy infection with malignant tertian rings. Antimalarial treatment was given at once, but the fever continued up to the 7th day, after which there was complete remission of fever. Since then the patient has had another transfusion of blood but has had no further attack of malarial fever.

The donor, a worker at the School, has been known to me for the last 8 years. He is an athlete, possesses a sound physique, and his bill of health has been quite clean. He had never before suffered from malaria, and physical examination revealed no enlargement of spleen or liver. He is one of our panel donors, and had donated blood on several occasions before without any ill effects either to himself or to the recipients. A permanent resident of Calcutta, he went out on a month's holiday to Fatehabad, Comilla, on the 3rd of March, where he stayed for nearly a month, and on his way back to Calcutta, he stayed at Comilla town from the 1st to the 4th of April, and returned to Calcutta on the 5th. He was quite fit on the 10th when I examined him prior to cross-matching his blood with the patient's blood. He donated 300 c.cm. of blood on 11th April, 1943, when he was reported to be in quite good health by Dr. T. K. Ghosh, the Physician in-charge of the patient. Later, the donor told me that, unlike previous occasions, this time he felt a little weak after donating his blood.

The donor had an attack of fever with slight rigor at about 10 a.m. on the day following the donation of blood, the temperature rising up to 103°F. in the afternoon. Examination of the blood next day revealed a moderate infection with malignant tertian rings. He was at once put on a course of antimalarial treatment by the doctor who examined him, and he was free from fever from 15th April, 1943. It was most unfortunate that he did not report his illness to me till

the 19th; he did not attend the School from 13th to 18th April, because these days were holidays. He had a relapse of malaria on the 4th of May, and examination of his blood this time also showed infection with malignant tertian parasites.

Comment

There can be no doubt that, in the case reported, malaria in the patient was transmitted through transfusion of blood from the donor. It is also almost certain that the donor was infected at Comilla, and that when he donated blood he was almost at the last stage of the incubation period. Donating 300 c.cm. of blood may have accelerated the attack of malaria in the donor by putting a large number of parasites into the peripheral circulation from internal organs such as the spleen; the contraction of that organ produced by hæmorrhage and the temporary lowering of the resistance of the patient on account of the loss of blood, probably hastened the onset of malaria. On the other hand, the number of parasites in the transfused blood was probably not low, since it was responsible for the production of heavy infection with malaria in the patient within the short period of 5 days.

Hutton and Shute (1939) are of the opinion that it is impossible to exclude malaria in a donor residing in the tropics, as 'chronic, latent or potential relapsing' cases cannot be diagnosed with certainty by any known method. In such cases of malaria, parasites may remain hidden in the internal organs for over 37 years (Jankleson, 1931) without producing any symptoms of malaria in the patient, or being detected in the blood at any time during these years. It is possible that after the sudden loss of 300 to 400 c.cm. of blood in such a carrier, the parasites will be forced from the internal organs into the peripheral circulation and thus be a source of danger both to the donor and to the recipient. Hutton and Shute working in England suggested the cancellation from the donors' list of anyone who had resided in the tropics, sub-tropics or Eastern Europe for short or long periods, whether with or without any attacks of malaria. The soundness of this view was very nicely demonstrated by the case reported by Nabarro and Edward (1939). In this case, 7 c.cm. of blood was injected intramuscularly into an infant from her father, and the child died subsequently of malaria. The donor, the father of the child, had a history of long residence in a malarious place in Ceylon, and though he was in the habit of taking quinine occasionally, he had never had any typical attack of malaria, and it was with the greatest difficulty that the parasites were demonstrated in his blood subsequently. It is thus abundantly clear that everyone of us living here may be a potential carrier of malaria parasites, and that blood from such a person is not suitable for transfusion to a patient without some preliminary treatment of the blood which would make it innocuous. That this statement is not a mere

hypothesis was indicated by Thoroughman (1940) who records a very high incidence of malaria through transfusion of blood from apparently healthy donors. He makes an analysis of 176 transfusions in 104 patients in Soochow hospital, Kiangsu, China, a malarious place. The patients were under observation for 15 days or more in the hospital after a transfusion of blood. Thoroughman found the incidence of malaria in the recipients to be 35.6 per cent, and that 21 per cent of individual transfusions were followed by the development of malaria in the recipients. In the 24 cases in which the results were clear cut, the shortest interval before parasites were found in the recipient's blood was 8 days, and the longest 20 days. The donors in these cases were mostly coolies of the place, who acted as paid donors. In most cases the blood of the donors was examined for malaria parasites before the donor was bled. The author is, however, very reticent about the previous state of health of the donors and their condition following the donation of blood which produced malaria in the recipients. Moreover the author does not give any information about the condition of the patient excepting that their 'initial' blood smear was negative for malaria. The incidence of malaria in the cases reported above appears to be unusually high. It may be possible that not all the cases of malaria in these patients were due to latent malaria in the donor. Incidentally it may be mentioned here, that in the course of last few months, since the management of the Civil and Hospital Transfusion Service was entrusted to us, altogether 257 transfusions were arranged for, in 60 cases with fresh citrated blood from the donors and in 197 cases with stored blood, the period of storage varying from 1 to 10 days. In all these cases this is the only occasion when malaria was reported to be transmitted from the use of fresh citrated blood. There can be no question of other similar accidents being missed by us, for with a very few exceptions, all the transfusions both with fresh and stored blood were given to patients in a hospital, and any case of malaria occurring in the patients after transfusion would have certainly been reported to us.

Attacks of malaria following transfusions of blood are reported by Thoroughman and others to be readily controllable by quinine, and excepting in the case of the child reported by Nabarro and Edward (1939) no death has been attributed to malaria acquired through transfusion of blood. This may be the reason why no serious attempt has been made even in India where the incidence of malaria is very high, to find out ways and means for the prevention of the transmission of malaria through the transfusion of blood. The present case, however, has led to the starting of a study of possible methods of preventing such accidents. Investigations are now in progress to find out if storage and/or treatment of blood with known antimalarial

drugs would prevent transmission of malaria through transfusion of parasitized blood.

Pending the finding of some such measure, other measures may be adopted to minimize the risk of transmitting malaria through transfusion of blood in this country. There are two different ways in which this may be attempted. First, as suggested by Hutton and Shute, prophylactic quinine may be given in doses of gr. x once a week regularly to all prospective donors. This method, however, is absolutely impracticable here. The other method is to give the recipients a course of quinine of gr. xv each day for 3 days following a blood transfusion. This method is recommended by Thoroughman, who reports that in 34 cases in which he gave prophylactic quinine in doses of 0.3 gm. three times daily for 3 days following a transfusion of blood, none of the recipients developed malaria, though he found an incidence of malaria of 35.6 per cent amongst untreated recipients of blood from similar donors. This second method appears to be reasonable and not impracticable and is according to Thoroughman's findings effective. I would, therefore, recommend that, for the present, a 3-day course of quinine gr. xv a day should be given to all adult patients receiving a transfusion of blood. Also the donor should be requested to report any illness occurring within 10 to 15 days of donating of blood, and any illness reported within that period should be thoroughly investigated, and if it proves to be malaria, a full course of anti-malarial treatment should be given to the recipient at once, irrespective of whether the recipient is showing any symptoms of malaria or not.

Summary

A case of malignant tertian malaria occurring in a patient on the 5th day after transfusion of blood is reported. This is the shortest known period in which malarial parasites have been found in the recipient after transfusion. The patient recovered from malaria with quinine treatment.

The donor also had developed malignant tertian malaria on the day following the donation of blood, from which he recovered after a course of quinine. The donor has since had a relapse of malaria.

Pending the introduction of some suitable measures for the prevention of transmission of malaria through transfusion of blood (this matter is being investigated), it is suggested that 5 grains of quinine should be given three times a day for 3 consecutive days to any adult receiving a transfusion of blood.

Acknowledgment

I am thankful to Dr. T. K. Ghosh, M.B., M.R.C.P., for supplying me with the notes of the patient.

(Concluded on opposite page)

'RECONSTITUTED SERUM' FROM BLOODSTAINS: ITS VALUE AND ITS LIMITATIONS

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Extracts of dry bloodstains in blood grouping tests.—Several years ago the writers failed in attempts to carry out blood grouping tests by the determination of the isohæmagglutinins (isonins) in material prepared from a dry bloodstain, by adding water or normal saline. This method of determining the blood group for forensic purposes was one of the earliest described (Martley, 1928). They thought the reasons for the failure were (i) a low isonin content of the blood in the tropics, (ii) a rapid deterioration of the isonins under tropical conditions, or (iii) the essential unreliability of the method. They were inclined to favour the last reason. Now they definitely know that the 'reconstituted' serum is not suitable for blood grouping tests.

The group of blood in dry stains is now usually determined by finding the isohæmagglutinogens (isogens) of the blood by absorption with known isonins.

Extracts of dried bloodstains in precipitin tests.—The defective nature of the 'reconstituted' serum has certain advantages. It makes it possible to use the precipitin test to differentiate human from simian blood in stains. In fresh serum it is difficult or impossible to do this. Sutherland (1910) wrote as follows:—

'Uhlenhuth has laid it down that ape's blood may be mistaken for human blood, so it was of great importance to investigate this point, although, so far as I am aware, it has not yet been

alleged in an Indian murder trial that the bloodstains in question had been caused by blood that had come from an ape, and not from a man, as alleged by the prosecution. Two reasons for this occur to me. One is that the Hindus revere the lungoor (*Semnopithecus entellus*). The other and more generally operative reason is that, even in India, the ape is not a domestic animal, and therefore is not at hand when most needed—by the defence: for Cicero's advice *causam mendaciumculis adspargere* is scarcely needed here in the East.

'Through the kindness of the Superintendent of the Calcutta Zoological Garden, and the Principal Medical Officer of the Royal Colonial Army of the Netherlands-Indies, I have been able to examine bloodstains due to the blood of the following varieties of the apes of the Old World* :—

Orang-utan—*Simia satyrus*,
Hooluck—*Hylobates niger*,
Siamang—*Hylobates syndactylus*,
Lungoor—*Semnopithecus entellus*,
Bonnet monkey—*Semnopithecus mitratus*,
Simpai—*Semnopithecus metalophus*,
Macaque—*Macacus cynomolgus*,
Pig-tailed monkey—*Macacus nemestrinus*,
Slender loris—*Nycticebus tardigradus*,
Rhesus monkey—*Macacus rhesus*.

'The stains were extracted in the usual way, and the extracts were diluted until they corresponded to 1 to 1,000 dilutions of blood sera. They were then all tested in a row, with many tubes of 1 to 1,000 dilutions of human sera and stain extract as controls. The rapidity and degree of reaction obtained in each tube were noted, when to its contents was added some anti-human serum of known specificity and potency. It was found that even in the case of the orang's bloodstain the reaction obtained was not "human", as it was not visible till after the expiry of twenty minutes; the human bloodstain extracts and dilute sera in each case reacted well before five minutes had elapsed. These experiments were repeated over and over again, the results being shown to those who did me the honour of visiting the laboratory, and in no case was a "human" reaction obtained with the extract of a simian bloodstain.'

The writers have repeated part of the work and agreed with the original findings.

A one-day old stain of blood of *Silenus rhesus* (the common monkey of India) on cloth fails to give a reaction, in a 1 in 1,000 extract: it gives a reaction in a 1 in 500 extract only. When one-week old, it fails to react even in this strength. In determining the presence of human blood in stains, errors due to group reactions

(Continued from previous page)

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* Not seen in original.

* Some of these names were not strictly correct when Sutherland wrote this in 1910, and some have been changed since. For example, *Macacus cynomolgus* is now usually called *Silenus irus*, and in general the name *Silenus* has replaced the name *macacus*.—Editor, I. M. G.

with simian blood can be safely excluded as long as a standard and well-controlled technique is adhered to.

Liquid simian serum, however, in a dilution of 1 in 1,000 reacts with antihuman serum very well. Here are the reactions of the human and simian sera with the two antisera :—

	Antihuman serum	Antisimian serum
Human serum, 1 in 1,000, in $\frac{1}{2}$ minute	+	—
Human serum, 1 in 1,000, in 3 minutes	+	+
Simian serum, 1 in 1,000, in $\frac{1}{2}$ minute	—	+
Simian serum, 1 in 1,000, in 3 minutes	+	+

The intensity of the reaction denoted by + was the same (the ring of the same size and colour). Observations before 'the expiry of twenty minutes' could not have differentiated one blood from the other.

The difference between the reactions of the liquid and the dried serum depends upon the nature of the 'reconstituted' dried serum. A 1 in 1,000 extract from the dried serum is definitely different from a 1 in 1,000 dilution of the liquid serum, though both have the same 'froth index'.

Incidentally it may be mentioned that the group reaction between ox or buffalo (taken together) and sheep or goat (taken together) is more difficult to exclude when the stains bearing the blood are tested by anti-ox or anti-sheep serum. They must be tested by both the sera to bring out the speed of the reaction. The result is based on the speed. Confirmation is obtained by dilution until one of the extracts fails to react. This confirmation is necessary.

The fact that the group reaction of the simian blood is lost in the dry stain makes it possible to test for human blood in stains from all over India. In one central laboratory, 18,271 such tests were done in 1941-42. The exclusion of a group reaction otherwise would need (i) comparison between two tubes of one stain every half a minute and (ii) dilution until the disappearance of reaction of one of the extracts.

Summary

The 'reconstitution' of serum from a dried bloodstain produces a fluid which is different from natural serum. The difference makes it impossible to determine the blood group from such a serum, but makes it possible to use the precipitin test to differentiate ape's blood from human blood.

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CHEMOTHERAPY IN CEREBROSPINAL FEVER: EXPERIENCE WITH SULPHATHIAZOLE IN A RECENT EPIDEMIC OF THE DISEASE IN OSMANABAD IN H.E.H. THE NIZAM'S DOMINIONS

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CEREBROSPINAL fever broke out in an epidemic form in Osmanabad town (population, 13,999) in the month of January 1942. During this epidemic there were altogether 50 cases definitely diagnosed as cerebrospinal fever. Of these 50 cases, 29 were treated as in-patients in the Infectious Diseases Ward of the Local Civil Hospital. Eleven cases were treated outside the hospital by isolating the patients, as far as possible, in their own houses. The remaining 10 cases either refused treatment of any kind or were treated by the local unqualified practitioners. Of this last group of 10 cases, 8 ended fatally, while out of 29 hospital cases only 2 died. All the 11 cases treated outside the hospital, but on the lines adopted for the hospital cases, recovered.

In all the cases coming under observation during this epidemic, clinical symptoms were of the usual type. The onset was abrupt, though in some cases there was naso-pharyngeal catarrh, nausea and slight malaise for a day or two before the onset of the more cardinal signs and symptoms. Pain in the muscles of the neck and the back, disturbances of mental faculties, and persistent headache were the main symptoms in most of the cases. The headache was generally localized to the occipital region. Rigidity of the neck muscles with pain on the slightest attempt at movement, particularly flexion, was present in all these cases, and in the severer cases the pain and the stiffness extended to the muscles of the back also. Retraction of the head and opisthotonos were seen in more marked cases. Kernig's sign was always present and the deep reflexes were exaggerated. In only 2 cases were petechial rashes seen; one of these ended fatally. One constant feature noticed in this epidemic was that herpes febrilis was present in every case, though in some cases the fever was neither high nor very prolonged. This herpes is said to be due to a specific virus activated by the disease.

Treatment.—Lumbar puncture was carried out in the first few cases for the purposes of diagnosis as well as for the removal of a small quantity of cerebrospinal fluid, but later this practice was abandoned, and immediately the patient was admitted to the hospital, or as soon as the clinical signs and symptoms warranted a diagnosis of cerebrospinal fever, the treatment with sulphathiazole by mouth was started.

On admission, 1 gramme of the powdered drug was given suspended in 3 to 4 oz. of water. This

was followed by another 1 gramme half an hour later. Afterwards for the first two days, or till the severity of the symptoms abated, 1 gramme of the drug four times during the day and twice during the night was administered in a similar manner. In the majority of cases, this intensive course was stopped after the first 48 hours, while in a few cases it was possible to reduce the dose even earlier. After the first intensive course, 0.5 gramme of the drug every 4th hour was continued for two or three days more. In children the dosage of the drug was reduced according to the age of the child and the severity or the mildness of the symptoms. In 75 per cent of the cases, the treatment was discontinued after the 4th day. In some cases, the drug caused

Harries and Mitman (1940) are of opinion that the sulphanilamide group of drugs should never be withheld from a case of cerebrospinal fever whether serum is administered or not. These drugs are given by the mouth, are rapidly absorbed, and are reported to appear in the cerebrospinal fluid in concentrations as great as in the blood. It is neither necessary nor advisable to use the intramuscular or intrathecal routes unless the patients are unable to take the drug by mouth.

Roche and McSweeney (1939) treated 11 cases of cerebrospinal fever with M.&B. 693 with 1 death. They also give their previous experiences with different methods of treatment. Their figures are interesting.

TABLE

Period	Method of treatment	Total cases treated	Cases recovered	Deaths	Percentage of deaths
1935-1936	Lumbar drainage and serum treatment.	36	9	27	75.0
1936-1937	Same as above together with prontosil album orally and soluseptasine intramuscularly.	56	24	32	57.1
1938-1939	M.&B. 693 orally; no intrathecal therapy.	11	10	1	9.1

severe nausea and vomiting, and a reduction in the dosage of the drug, an increase in fluids by mouth and an alkaline mixture were generally able to control these symptoms. In 1 case, anuria developed on the 3rd day. Immediate stoppage of the drug, plenty of barley water and an ordinary diuretic mixture helped to avert the danger. Constipation was the rule in all cases, and was treated by ordinary soap enemata. Diet during the period of the administration of the drug as well as during the acute stage of the disease consisted of milk alone or milk and sago. Barley water was given freely whenever the patient could take or relish it.

Results of the treatment.—As mentioned above, all cases treated on the above lines but in their own houses recovered. Of the 29 cases treated in the hospital, 2 died and 27 recovered. These 2 fatal cases had been admitted into the hospital in a moribund condition, and died within few hours of their admission. The details regarding the 29 cases treated in the hospital are given in the accompanying table.

Discussion.—Walsh (1938) reviewed 23,685 cases occurring between the years 1920 and 1936 and concluded that there was no evidence that the use of specific serum in cases of cerebrospinal fever had lowered the case fatality in recent years. In the Campbell Hospital, Calcutta, out of 636 cases treated with serum there were 436 deaths (Kapur *et al.*, 1934). In this instance serum prepared from the local strains is reported to have been used.

Chemotherapy has nowadays revolutionized the treatment of meningococcal infections.

Previous to this, Schwentker, Gelman and Long (1937) used M.&B. 693 in 10 cases, and reported that this line of treatment was good and quite comparable to that given by the specific serum therapy. They had only 1 death in this series of cases.

Sprockhoff is reported to have treated 15 cases on these lines with 2 deaths (Underwood, 1940). Similarly Osborn (1939) treated 3 cases with sulphapyridine, and all of them recovered.

Experience of workers in the Anglo-Egyptian Sudan gives further evidence of the efficacy of chemotherapy in cerebrospinal fever. Somers (1939) reported that in Anglo-Egyptian Sudan during the period 1934-1938 there were 21,599 cases with 14,816 deaths, giving a case mortality of nearly 68 per cent. At the beginning of the year 1939 and before the commencement of the treatment with sulphapyridine, there were 41 cases with 33 deaths. The subsequent cases, 143 in number, were treated with small doses of sulphapyridine. The case mortality in this last series was only 10 per cent.

Bryant and Fairman (1939), in an outbreak of cerebrospinal fever among the Dinkas of Sudan, treated 21 cases under field conditions, with prontosil and tablets of sulphanilamide. There was only 1 death. In the same outbreak, 168 patients were treated with M.&B. 693 in saline suspension, and there were 8 deaths (2 did not react to the drug, 2 were epileptics, and in 3 cases the treatment was started very late in the course of the disease). The percentage of recoveries in this series of cases was 95.2. According to these workers, recovery was directly proportional to the quantity of the drug

administered and the rapidity with which the patient was brought under treatment.

In England, excluding untreated or inadequately treated cases, Banks (1939, 1940) had only 1 death in 80 consecutive cases treated by chemotherapy (sulphapyridine and sulphanilamide) alone. Emphasis is laid on the necessity of adopting a high initial dosage and giving subsequent doses according to a prescribed scale depending on the age of the patient.

Summary and conclusion.—A study of recent literature on the treatment of cerebrospinal fever shows that by far the best results are obtained by chemotherapy. Serum alone or combined with chemotherapy does not show as good results as chemotherapy alone. The treatment so far has generally been carried out either with sulphapyridine (M.&B. 693) or sulphanilamide; the evidence is slightly in favour of sulphapyridine.

and are definitely superior to those obtained with specific serum alone or in combination with other drugs.

Toxic symptoms arising from the use of sulphathiazole are few and can be controlled or treated by simple routine methods.

My thanks are due to Dr. M. Farooq, Deputy Director, Public Health Department, for supplying the necessary quantity of sulphathiazole for the treatment of these cases, and to Mr. Mustafa Ali Khan, District Collector and President of the Osmanabad Municipality, for kindly erecting a temporary ward in Civil Hospital, Osmanabad, for the isolation and treatment of the cases of cerebrospinal fever. My thanks are also due to Dr. (Mrs.) Indira Bai Pathak, the Lady Sub-assistant Surgeon in the hospital, for carefully looking after and nursing the female patients of cerebrospinal fever admitted into the hospital.

Statement showing details of the cases of cerebrospinal fever treated with sulphathiazole in the Civil Hospital, Osmanabad

Serial number of the patient	Age in years	Sex*	Duration of the stay in the hospital	Day of the disease on which the treatment commenced	Total quantity of sulphathiazole used in grammes	Result	Diagnosis, clinical or bacteriological
1	25	M.	10 days	4th	25	Cured	Bacteriological.
2	20	M.	8 "	3rd	19	"	Clinical.
3	45	F.	12 "	4th	18	"	"
4	6	M.	6 hours	6th	3	Died	Bacteriological.
5	18	M.	5 days	3rd	11	Cured	Clinical.
6	19	M.	8 "	3rd	17	"	Bacteriological.
7	20	F.	9 "	4th	16	"	"
8	8	F.	11 "	2nd	14	"	Clinical.
9	11	F.	7 "	2nd	14	"	"
10	20	M.	7 "	3rd	22	"	Bacteriological.
11	6	F.	5 "	3rd	6	"	Clinical.
12	10	F.	9 "	2nd	10	"	"
13	9	F.	9 "	3rd	9	"	"
14	12	F.	8 "	4th	8	"	"
15	36	M.	5 "	2nd	10.5	"	"
16	30	F.	11 "	3rd	11	"	"
17	4	F.	6 "	1st	5.5	"	"
18	10	F.	6 "	2nd	7	"	"
19	14	F.	25 "	5th	22	"	"
20	50	F.	9 "	2nd	20.5	"	"
21	4	M.	5 "	5th	5	"	"
22	20	F.	6 "	6th	11	"	"
23	8	F.	7 "	3rd	4.5	"	"
24	9	M.	2 hours	6th	1.5	Died	"
25	11	F.	5 days	2nd	6	Cured	"
26	6	M.	4 "	2nd	5	"	"
27	25	F.	5 "	2nd	13	"	"
28	30	F.	10 "	3rd	14	"	"
29	50	F.	6 "	2nd	10.5	"	"

* M. = Male.
F. = Female.

In the present series of cases, sulphathiazole alone has been used. Excluding the 2 fatal cases in which only a small quantity of the drug could be administered, the average quantity of sulphathiazole used in treatment was about 14 grammes. This is less than the quantity of M.&B. 693 recommended for a case.

The results of treatment with sulphathiazole are in every way comparable with those obtained either with sulphapyridine or sulphanilamide,

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A Mirror of Hospital Practice

A CASE OF MUSHROOM POISONING

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Assistant Doctor

(From the Dima Hospital, Kalchini, Jalpaiguri)

MUSHROOMS are occasionally used by the tea garden labourers as a food. On the 12th April, 1943, a female garden labourer aged about 38 years came to the hospital in a condition of extreme intoxication, being supported by her husband. She had taken some rice and cooked mushroom in the morning, and developed the condition about half an hour after taking the food. Within 10 minutes of arrival at hospital she began to develop the symptoms of acute mushroom poisoning with profound excitement, intoxication, delirium with stupor and occasional convulsions. The pupils were contracted, and there was frothing at the mouth and nostrils.

Emetics were given at once, and in time the woman vomited all the stomach contents consisting of food and particles of cooked mushrooms. An injection of atropine was given as an antidote, and with some stimulants and warmth the patient had an uneventful recovery within 8 hours.

Our thanks are due to Mr. C. M. Slaughter, the manager, for his keen interest, and Dr. W. G. Cattell, the C.M.O., for his kind permission to publish the note.

SCURVY IN BILASPUR STATE

By BRIJ LAL BATRA, L.S.M.F. (Pb.)

Medical Inspector and Officiating In-Charge, Sir Bije War Memorial Hospital for Women, Bilaspur State, Simla Hills

BILASPUR STATE is a hill state, in the Simla hills. Its area is 452 square miles; the average altitude is 3,000 feet though some of the hills rise to a height of 6,000 feet or over. Most of the land is under cultivation, and the crops generally grown are maize, wheat and rice. The source of irrigation is chiefly rain water. The staple diet of the public is maize and dal, with occasionally wheat, rice, fish, meat and vegetables. I have come across many cases of

vitamin-deficiency diseases here, the chief being pellagra, and second to it is scurvy. I have come across scurvy more commonly in females. The cases treated have been between the ages of 20 and 45. The cases have been seen at all seasons.

All cases improved with the administration of good food and vitamins. An account of 16 cases is given. They have been divided into two groups—severe and slight.

Severe cases

Only three cases are allotted to this group. All were treated as in-patients.

Case 1.—Hindu female, married, aged 27. The symptoms in this case were not typical of scurvy but the case was put in this group due to the severity of symptoms. The patient complained of the passage of blood in the vomit and in the stools. There was loss of appetite, weight had decreased, and there was progressive weakness. She had constant headache. The gums were healthy. There were no subcutaneous effusions under the skin. There was cardiac distress. The case was diagnosed as one of peptic ulcer and was treated on those lines by me with no improvement. Sometimes the number of vomits was very large and in all vomits there was a certain amount of blood. She was put on alkaline mixture with hæmostatic serum with no improvement. On the 11th day after admission, she began to get bleeding from the eyes—sometimes from one eye and sometimes from the other. It could not be judged precisely where the blood came from, but bleeding was profuse. There was much depression.

Treatment.—The patient was put on a well-balanced diet. She was given raw onions, raw tomatoes, some cooked vegetables, plenty of milk and fruits.

She was put on a tonic mixture along with eivitin (P. D. & Co.) injection 2 c.cm. daily and civibex tablets 6 daily. With the fourth injection, the bleeding from the eyes stopped, and on the 11th day the number of vomits was much reduced until they stopped on the 15th day. The injections and tablets were stopped but the tonic mixture was continued with good diet. She was discharged as cured 1½ months after admission. It was reported that since discharge she gets a recurrence of vomiting from time to time.

Case 2.—Hindu female, wife of an agriculturist; duration of complaints 15 days. She complained of swelling of the gums with bleeding. There were painful subcutaneous effusions in both the legs. The patient was unable to walk. She also complained of loss of appetite and constipation.

Treatment.—The patient was put on a well-balanced diet and civitin injections with civibex tablets. For the mouth condition she was given hydrogen peroxide gargles and silver nitrate 2 per cent paint on the gums.

Patient left the hospital against advice with very little improvement.

Case 3.—Hindu female, aged 45. Hers was the most typical case. The duration of complaints was 4 months.

Complaints.—Progressive weakness, pallor, loss of weight, duration 4 months. Feeling of cramps and stiffness in the legs and inability to walk, duration 3 months. The gums were swollen and spongy and the

teeth were shaky. Even with the slightest pressure on the gums, there was much bleeding. The salivary glands were enlarged, and the breath was very foul. The skin was dry and rough and there were subcutaneous effusions on the legs, thighs and near the elbows. The knee joints especially were stiff. There was cardiac distress with a hæmic murmur near the apex. The urine was full of albumin. The patient had occasional headache and slight constipation. She was melancholic.

Treatment.—When brought to hospital, the patient was put on a well-balanced diet with raw tomatoes, raw onions, plenty of milk and ghee. She was also given cooked germinated gram. Of citrus fruits, she was given oranges, and as fresh lemons were not available, she was given lemon *achar*. She was given a tonic mixture, civitin injections 2 c.cm. daily and civibex tablets 6 daily for 15 days. For the gums, she was given hydrogen peroxide gargles with 2 per cent silver nitrate paint.

On the 7th day the patient noticed improvement; there was diminished stiffness in the legs, and the subcutaneous patches began to fade. From the 10th day the bleeding from the gums became less. She could walk a little on the 15th day. Slowly the bleeding from the gums completely stopped. Later the depression disappeared. The patient is still under treatment, and is progressing.

Slight cases

Thirteen cases are put in this group. Four cases had bleeding gums and weakness. They were first treated as cases of pyorrhœa but later were put on well-balanced diet with civibex tablets internally. Three of them improved but one discontinued the treatment.

Five cases had subcutaneous effusions with pain in the legs. Two of them were put on a well-balanced diet and civitin injections. Unfortunately these cases did not carry on the treatment and did not report regularly. Four had bleeding gums and slight effusions under the skin. They all improved under dietetic treatment.

Summary

Sixteen cases of scurvy are reported and details of three cases are given. Those treated with a well-balanced diet plus administration of vitamins showed improvement.

A CASE OF CHEST INJURY EXPOSING PLEURAL CAVITY AND LUNG

By G. C. PATTANAYAK, M.B., B.S., D.T.M.

Orissa Medical Service, Sub-Divisional Hospital, Angul, Orissa

A FEMALE child, aged 11, was admitted into the hospital with an open injury of the chest. The child had been gored by a buffalo a few hours before. The site of the injury had been bandaged with a dirty cloth. She was brought in a bullock cart from a distance of 5 miles. There were no signs of shock. At operation under general anaesthesia, a wound 2 inches by

1½ inches was found on the sixth left intercostal space near the mid-axillary line. The pleural cavity was exposed. Air was rushing in and out with respiration, with a peculiar hissing sound, and the dome of the diaphragm and the lower margin of the lung were seen moving up and down with expiration and inspiration. There was no subcutaneous emphysema. No blood could be seen in the pleural cavity. The margins of the wound were freely excised including the torn pleural margins. During the excision of the pleural tissues, respiration suddenly stopped, probably because of pleural shock. Respiration restarted under ordinary artificial respiration. To combat further pleural shock, morphine hydrochlor gr. ¼ was injected intramuscularly with atropine sulphate gr. 1/150. No further respiratory trouble occurred. Sulphapyridine powder was introduced into the pleural cavity, and sprinkled in the excised wound. Two tension sutures were introduced. The wound was closed by three layers of buried catgut sutures securing pleural, muscular and subcutaneous tissue margins. A gauze dressing was kept in position by the tension sutures reinforced by two strips of leucoplast. With a looped chest bandage the patient was put to bed. Tetanus antitoxic serum, 1,500 international units, was injected during anaesthesia. The patient had an uneventful recovery; the stitches were removed on the seventh day after operation. There was no sepsis; the wound healed by first intention. The chest movements and breath sounds were normal from the second day onwards. On the eleventh day after admission, the patient was discharged.

A CASE OF ANEURYSM OF THE TRANSVERSE PART OF THE ARCH OF AORTA

By A. R. SEN, M.B., B.S.

Medical Officer In-Charge, Municipal Hospital, Amalner (East Khandesh), Bombay Presidency

L. N. T., aged 55 years, a business man by occupation, came to me for the treatment of following complaint; pain on the left side of back, radiating down towards the left, duration two years.

History of the case.—For the last two years, the patient has been experiencing pain on the left arm. The pain is dull in character commencing from the region of left side of back (infra-scapular region) down the whole of the left arm. At times, the pain becomes very severe and acute, resembling almost an 'electric shock', but such pain lasts for only a short time. He does not give any history of syphilis. During the last two years he has consulted at least half a dozen doctors at various places, but none could relieve his malady.

On examination.—Pulse—80 per minute; respiration—20 per minute. The temperature was normal. Teeth—a few left; teeth have been removed for pyorrhœa alveolaris. Epitrochlear glands were palpable. Throat,

tonsils and pharynx were normal (no evidence of any septic foci). Heart sounds were normal in all the four areas excepting the second sound in aortic area which was slightly accentuated (?). Blood pressure were 120 systolic and 80 diastolic. The lungs were clear and the abdomen was normal and soft.

Reflexes—knee jerks, biceps jerks normal. Sensibility to pin-prick normal all over the body.

Urine examination.—Specific gravity—1018; acid reaction; sugar and albumin—nil.

Wassermann reaction could not be done due to lack of laboratory facilities.

A provisional diagnosis of 'neuralgia' was made by me, and I put him on symptomatic treatment for about a month but he had no relief. The patient insisted on a skiagram of the chest (in fact he had been insisting on this from the very beginning). Merely to satisfy him, a screening of the chest was done.

Screening and x-ray report. A deep-seated, small aneurysm at the transverse part of the aorta.

The diagnosis now became complete. The nature of the pain can now be explained. I re-examined the patient. The blood pressure was different on the two sides: right side—120/80; left side—100/76. The tracheal tugging test was positive.

There was absolutely no pulsation visible either in front or at the back of the chest. The accentuation of the second sound in the aortic area could now be explained.

The patient was put on potassium iodide and calcium lactate, and the diet was restricted; some relief of pain was obtained.

Ten months later the patient was under ayurvedic treatment and was showing all the classical signs of aneurysm of the aorta, with marked pulsation and pressure symptoms.

Points of interest.—(1) A diagnosis of a small, deep-seated aneurysm is difficult unless x-ray is done.

(2) In early cases of small aneurysm, the typical signs and symptoms are absent. In this particular case, there were no signs and symptoms present other than the pressure symptoms on intercostal nerves and accentuation (?) of the second sound in the aortic area.

Acknowledgment.—My thanks are due to Dr. N. V. Mhaskar for the x-ray report.

A CASE OF HÆMOTHORAX

By B. L. CHOPRA, L.R.C.P., L.R.C.S., L.M., D.P.H., D.T.M.
Divisional Medical Officer, N.-W. Railway, Ferozepore

A GANGMAN was admitted into Ferozepore Railway Hospital on 25th February, 1943, suffering from an injury of the left side of the chest. The left side of the chest was found immobile on respiration and the intercostal spaces appeared to be slightly bulging; there was dullness on percussion and no vocal fremitus could be elicited. It was further discovered that there was a fracture of the 9th rib on this side. Hæmorrhage of the left side was suspected as a result of the fracture of the 9th rib and this was confirmed by x-rays (see figures 1 and 2, plate XX).

Aspiration of the fluid was undertaken and about 10 ounces of blood were drawn off, giving the patient considerable relief. After 3 days, however, he again complained of heaviness, and it appeared that some blood was left. Calcium was given and absolute rest was ordered. With this treatment, breath sounds and vocal fremitus again became normal over most of the area except for a narrow strip of dullness.

Aspiration was repeated, and an ounce of blood was withdrawn. The man made an uneventful recovery and was discharged cured 6 weeks after his injury.

This case is interesting as it brings about the following facts:—

1. That blood when effused in the pleural cavity does not as a rule clot *en bloc*, but the fibrin is deposited as a layer over the parietal and visceral pleura as a result of churning movements of respiration.

2. That a small hæmorrhage (that is, one about a hand breadth in length) may usually be left to the natural powers of absorption, and if it does not quickly decrease, aspiration should be employed.

3. A large hæmorrhage with fluid blood present should always be aspirated early, and, if necessary, the aspiration must be repeated and the removed fluid replaced by air.

The exudate was examined under the microscope and no pus was found; otherwise open operation with a view to emptying the cavity completely would have been undertaken. The presence of a large hæmorrhage with clotted blood which cannot be withdrawn through an aspirator is also an indication for thoracotomy, which should consist of removing about 4 inches of a rib suitably situated, so as to permit the introduction of a retractor or rib spreader.

My thanks are due to Dr. C. D. Newman, Chief Medical and Health Officer, N.-W. Railway, Lahore, for his permission to publish this note.

SCIATICA AND ITS TREATMENT BY SALINE INJECTIONS ROUND THE NERVE

By B. L. CHOPRA, L.R.C.P., L.R.C.S., L.M., D.P.H., D.T.M.
Divisional Medical Officer, N.-W. Railway, Ferozepore

In two different parts of North India I have found sciatica to be common, and I have used in treatment the method described by me in 1938 (Chopra, 1938).

The treatment consists of giving an injection of four to eight ounces of normal saline solution at a temperature of 104°F. round the sciatic nerve near where it leaves the pelvis.

The site of the sciatic notch was found by drawing a line from a point midway between the outer border of the ischial tuberosity and the posterior superior angle of the greater trochanter to the upper angle of the popliteal fossa; the uppermost posterior point of this line was taken as the site for injection into the nerve.

A lumbar puncture needle was used for the purpose of injection. As soon as the needle

touched the nerve, sharp pain along the whole course was felt. The needle having been steadied at that point, four to eight ounces of normal saline solution at a temperature of 104°F. were injected from a 30 c.c. syringe.

The injections were given twice a week. Two or three injections were usually needed to affect a cure.

Acknowledgment

My thanks are due to Dr. C. D. Newman, Chief Medical and Health Officer, N.-W. Railway, Lahore, for allowing me to publish this note.

REFERENCE

CHOPRA, B. L. (1938) .. *Antiseptic*, 35, 329.

STRANGULATED HERNIA WITH AN UNUSUAL HISTORY AND COURSE

By S. R. GORUR, M.B., B.S. (Bom.)

District Medical Officer, Kolar District, Kolar

A HINDU MALE, aged 45 years, was admitted into the district hospital here for the treatment of a lump over the scrotum of the size of a coconut, discharging faecal matter through an opening.

Previous history

The patient had gonorrhœa five years ago. It was treated by a *void*. The discharge stopped but subsequently there developed difficulty in micturition. Later, the patient observed swellings on both sides of the groin which became more prominent during any strain, and disappeared when he lay down. The one on the right side became very prominent, reaching the level of the bottom of the scrotum and at times he had to manipulate to force the contents back into the abdomen. Such reduction was accompanied by a gurgling sound.

Present history

Six months prior to the admission, the patient felt a little pain over the right groin and he saw that the swelling was much bigger than usual. The pain was not so bad as to disable him or to make him seek medical aid. The pain persisted for a few days, during which he was advised by *voids* to use local applications and fomentations. Throughout this period, he had neither vomiting nor constipation. He continued his usual diet, though in smaller quantities. A fortnight later, he suddenly found a little pus and some greenish yellow semi-solid matter of faecal smell escaping from an opening in the swelling above. This discharge gave him a little relief. Subsequently he observed that the continuous discharge above the scrotum was irritating the skin and preventing his work. About a week before admission, during an act of straining he observed a large mass protruding through the opening and lying above the scrotum completely covering it. This

made him nervous and hence he sought admission into the hospital for treatment.

Examination.—The patient was a lean built individual of average health. Pulse 80; respiration 22; temperature normal.

In the right inguinal canal there was fullness which would become tense and prominent on straining, or standing. Beyond the external ring, there was a mass consisting of a coil of prolapsed small gut rolled up to a size of a coconut and covering the whole scrotum in front. There was an opening through which semi-solid greenish yellow faecal matter was escaping. The skin of the scrotum underneath the mass was excoriated and red due to this discharge.

On the left side there was a slight hernia.

On admission the patient was put into bed with the foot of the bed raised to facilitate the return (reduction) of the prolapsed mucous membrane through the big fistular opening. Thirty grains of pulvis cretæ aromaticus were administered thrice a day to make the faecal flow through the fistula a little thick and less irritant. An enema was given on alternate days to clear the lower bowel. On the third day after admission, the prolapsed gut was partly reduced, and on the fourth day it had completely disappeared and only the faecal fistula was seen above the scrotum. This satisfied the patient and he agreed to undergo surgical treatment to cure the trouble which had now lasted about seven months.

X-ray photographs were taken after a barium meal and enema. Most of the meal passed through the fistula, and the cæcum and the colon remained practically empty.

Lister's bougies were passed into the urethra and its patency was found to be nearly normal.

It was intended to resect the involved portion of the gut, make an anastomosis, and repair the inguinal canal, all at one sitting. The upper part of the inguinal canal was clean and the internal ring was wide enough for the necessary manipulation. Hence, the approach was made by an incision over this region after protecting the infected serotal area with sterilized towels.

The sac was isolated near the neck and opened. It was found that the cæcum was lying in the inguinal canal with the appendix nicely walled off from the peritoneal cavity, by adhesions. At the apex of the appendix was the opening by which the faeces were escaping. The terminal part of the ileum and commencement of the ascending colon were brought to the surface, and an end-to-end anastomosis was done after the resection of the involved part of the gut. The part and its surroundings were well dusted with sulphanilamide powder and returned to the abdominal cavity. The portion of the hernial sac near the neck was dissected out from its surroundings, was transfixed and transplanted.

The incision was extended over the scrotum, and the affected loop of gut was dissected and removed. The inguinal canal was obliterated, and the wound was closed, each layer having been well dusted with sulphanilamide powder.

A drainage tube was put in at the lower part of the incision over the scrotum and was removed after 48 hours.

Convalescence was remarkably uneventful. The stitches were removed on the tenth day and the patient took his usual food from the fifteenth day. He was discharged on the sixteenth day after operation.

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Indian Medical Gazette

AUGUST

HYPOVITAMINOSIS

From time to time we have published in this journal articles on vitamin deficiencies in India, and although it seems that some interest is being taken in the subject, it is a fact that poverty, ignorance, conservatism and indifference remain formidable obstacles to progress. It is obviously necessary to make India more nutrition minded in order to improve the general physical and mental state, although the subject is closely associated with other important problems such as the development of agriculture, prevention of malaria, etc. The valuable investigations carried out by various workers seem to indicate that India suffers mainly from vitamin-A and B-complex deficiencies. Vitamin-D deficiency is less common than in other countries where the sunlight is not so active, whereas vitamin-C deficiency becomes prominent only under certain conditions. We propose here to draw attention to some early manifestations of vitamin deficiencies because their incidence is perhaps greater than is thought, and they are liable to pass unnoticed as they are less obvious.

Nyctalopia, poor vision in dim light, often called night blindness, is an early sign of vitamin-A deficiency. Common complaints are stumbling in dim light, difficulty in finding a seat in a darkened hall, or in driving a car at night. There are no obvious changes in the fundus oculi, and the day vision is normal or can be corrected by glasses to normal. Night blindness may however be caused by other conditions, such as retinitis pigmentosa, hysteria, etc.

In the next stage of vitamin-A deficiency, changes appear in the conjunctival epithelium. It becomes smoky in colour, shows pigmentation and wrinkling, and loses its normal lustre. If the eyelid is held open for a few minutes, the surface of the eye gets dry quickly. Itching, burning and photophobia occur, and Bitot's spots may appear. These spots are triangular patches of foamy yellowish-white exudate situated in the palpebral fissure, usually on the temporal side of the cornea. Later, there is diminished sensitiveness of the cornea which gradually turns hazy.

Dryness of the skin and hair may be the early symptoms of vitamin-A deficiency. Follicular keratosis develops, the hair follicles are enlarged, and the condition is sometimes called toad's skin (phrynoderma). The small eruptions are discrete, tend to appear in groups, and are more or less symmetrical in distribution, involving chiefly the external surface of the thighs and the forearms near the elbows. To the examining finger they give the sensation of

passing over a rough surface. The general nutrition of these individuals is usually poor. Vitamin-A deficiency may also cause atrophy of the enamel of the teeth, leading to caries.

The early symptoms of vitamin B₁ (thiamin) deficiency are vague and non-specific; nevertheless they are important because they are found frequently, a large proportion of the population being on the border-line of deficiency. Loss of appetite, weight and strength is one of the first observable manifestations. Various symptoms develop pertaining to the digestive, circulatory and/or nervous systems. Typically the onset is gradual. There may be indefinite abdominal pain, atonic dyspepsia and constipation. Myocardial dysfunction giving rise to palpitation, shortness of breath, weakness and perhaps oedema of the ankles may be evident. Subjective sensations of burning in various parts of the body, numbness, tingling, 'pins and needles' and muscular cramps are common. There may be headache, vertigo and faulty vision. A neurasthenic syndrome, e.g. undue anxiety, mental depression, insomnia, forgetfulness and early fatigue, has been described. Tenderness of muscles especially of the calves, weakness and heaviness of the legs and neuralgic pains are not uncommon; they are more marked in chronic alcoholics and in pregnant women.

Symptoms due to deficiency of certain members of the B₂ complex are also frequent. Riboflavin deficiency particularly affects the eyes, lips and tongue. There may be congestion and proliferation of the minute blood vessels round the cornea; these changes later tend to spread to the cornea. The oral lesions are preceded by burning and soreness of the lips and tongue. The discomfort may be severe enough to interfere with eating and swallowing. There is erosion of the mucous membrane of the lips which look more red than normal, and cheilosis (angular stomatitis) develops. In a typical case, white patches are visible at the angles of the mouth, the epithelium on this area having a sodden appearance. The patches may extend inwards to the mucous membranes of the cheek. Radiating fissures are often present. The tongue is red and glazed (magenta red) with a clean surface, sometimes fissured. In some cases there may be seborrhœic dermatitis of the alæ nasi and on the chin and malar prominences.

Another fraction of the B₂ complex, nicotinic acid, plays an important part in the prevention and cure of pellagra, although it may not be the only factor which is concerned in this disease. There is a long prodromal period, in which symptoms somewhat resemble those of thiamin and riboflavin deficiency. The tendency to seasonal recurrence or exacerbation of symptoms is however very suggestive. There is reason to believe that sub-clinical cases far outnumber those of clinical pellagra, but their detection is difficult. The nervous symptoms occasionally precede any other symptom by weeks or months,

and in such cases diagnosis can be made only by a therapeutic test.

Another manifestation of B-complex deficiency is dysfunction of the small intestine, which may give rise to nutritional diarrhoea and anaemia. This process plays a part in the aetiology of non-specific diarrhoea and para-sprue conditions.

While definite evidence of vitamin-C deficiency is not commonly seen, there is perhaps a considerable prevalence of hypovitaminosis, but the symptoms are vague and not pathognomonic. A child for instance is disinclined for food, ceases to thrive, loses its healthy appearance and becomes pale. Or perhaps a child is brought to the doctor on account of screaming when the limbs are touched or for frequent bruising of the skin, particularly on the face. In adults the symptoms are weakness and lassitude, dizziness on standing, and bruising or bleeding from the gums on slight trauma. There is pain in the legs, and the calves may appear hard. Follicular keratosis may be an early sign. A study of diet and laboratory tests such as the saturation test seems to show that symptomless deficiency really exists, and that many people are in a sub-scurvy state. The symptoms often remain latent until an infection supervenes or an individual is wounded or operated on; then the wounds heal very slowly and ulcers are apt to bleed.

The vitamin-D requirements of the body vary markedly with age, growth, pregnancy, etc. The manifestations of deficiency also vary widely and at different ages, and with different degrees of deficiency. In general, the early symptoms are mild and indefinite, coming on insidiously, and may escape detection unless checked by x-ray and biochemical studies of the blood, backed by a therapeutic test. Nervous irritability and excessive head sweating especially at night are indications of vitamin-D deficiency in a child. He may suffer from diarrhoea, bronchitis, convulsions, tetany or laryngismus stridulus; or advice may be sought for delay in dentition, in speaking or in walking. Frank rickets is not commonly seen in India, and is rare in Indian children. The children of fussy European or Anglo-Indian parents who are afraid of exposing their children to the sun sometimes develop frank rickets. In adults, osteoporosis may develop, especially during or after pregnancy. However, these are, in the light of our present ideas of the deficiency, late signs.

The above is a general description of the main individual vitamin deficiencies, but in actual practice there are many difficulties; multiple vitamin deficiencies are frequent, and their symptoms and signs often overlap, so that it is not always easy to trace the particular food factor responsible for the clinical manifestations. Thus an individual gets easily tired and has loss of appetite—this may be the earliest symptom of both vitamin-B and -C deficiencies. Follicular keratosis may be induced by deficiency of A, C and possibly B₂ complex. The development of

perfect teeth and the prevention of dental caries are dependent on an intake of adequate amounts of A, C and D as well as calcium. Thus the deficiency is seldom single. If a diet is deficient in one essential, it is apt to be deficient in others; hence even if one clinical syndrome dominates the clinical picture, multiple deficiencies are often present, although to a less degree. This dictum does not always hold good, for with a diet apparently grossly deficient in many factors, only a single clear-cut deficiency syndrome may be apparent. Moreover individuals living on more or less the same kind of deficient diet may develop quite different syndromes. Our present knowledge cannot satisfactorily explain these anomalies.

In diagnosing hypovitaminosis, it is most important to enquire minutely into the patient's diet. Certain laboratory tests are very useful, and it is sometimes necessary to resort to therapeutic trials. It should be emphasized that a sound natural diet has sufficient vitamins to meet all ordinary requirements. The normal person on a sound natural diet does not need all kinds of vitamin preparations put up in a fancy way at a fancy price. This 'vitamin ramp' as it has been called should not be encouraged by the medical profession, nor should the physician order patent vitamins unless there is a real need for them. In illness, particularly acute illness, supplementary vitamin may be needed, but a deficient diet should be corrected by giving adequate quantities of natural foods. For an Indian it is possible to ensure good health and nutrition on diets composed of whole or under-milled cereals, milk and its products, green leafy vegetables, pulses and fruits, with or without a little meat.

R. N. C.

Medical News

AIR RAID PRECAUTION SERIES: MEDICAL MEMORANDUM AND MEDICAL MANUAL

THE following are some of the series on air raid precautions prepared for Civil Defence Department, Government of India:—

MEDICAL MEMORANDUM No. 1 (INDIA): *Emergency Hospital Equipment.*—This is meant for the guidance of medical officers in organizing emergency hospitals. A unit of 100 beds has been taken as a working basis. The pamphlet gives a list of equipment necessary for such a unit, divided into sections according to the particular branch of surgery, etc. It also deals with storage and care of surgical instruments and appliances, use of cotton as suture material, and discusses the establishment (medical, nursing and other staff) of an emergency hospital.

MEDICAL MANUAL No. 1 (INDIA): *Medical Treatment of Gas Casualties.*—This booklet presents facts with which doctors engaged in Civil Defence Organization should be familiar. It gives a concise account of war gases with special reference to their general properties, symptoms and treatment. The essentials of a 'cleaning

section' of a first aid post are represented diagrammatically, and a diagnostic chart with a table of common war gases is given at the end.

MEDICAL MANUAL No. 2 (INDIA): The Training and Work of First Aid Parties.—It cannot be too strongly stressed that training is essential to success. This manual has been issued to assist in the training and work of the first aid parties, and most of the informations given are based on experience gained in different theatres of war. The first aid treatment of fractures, hemorrhages, burns, etc., has been simplified, keeping in view the greater importance of rapid and comfortable removal of the casualty to a place where he can obtain proper care and treatment. It has been emphasized that to achieve success individuals and parties should co-operate and work together as a team.

AUXILIARY NURSING SERVICE: RELAXATION OF AGE LIMITS

To enable young women to undertake training for General Service under the scheme for the Auxiliary Nursing Service, India, it has been decided to reduce the lower age limit for admission from 18 to 17½ years. The upper age limit, which is 45, is relaxable in the case of those who are physically fit and otherwise suitable.

FATIGUE AND EFFICIENCY IN FACTORY WORKERS UNDER PRISON CONDITIONS OF LABOUR

We have received a copy of the above reprint from the Coimbatore District Medical Association Annual, 1942. It gives an account of the details of study made by Colonel Karamchandani on industrial fatigue among the convict labour in the cotton manufacturing department of the Central Jail, Coimbatore. Special measures such as extra attention to general hygiene, hours of work, comfort, etc., were adopted to reduce the depressing effect, and the output, it is said, was thereby distinctly increased.

THE POLICY AND PROGRAMME OF THE CALCUTTA BLOOD BANK

The policy of the Calcutta Blood Bank is to collect and supply blood and serum to meet the transfusion needs of all sections of the community. There is no discrimination between the needs of the civilian and the military population or between the Indian and European groups. However, any individual or group of donors may designate, if they so choose, how they wish to have their donations utilized.

The hazards of the present military operations may at times make very pressing and immediate demands for a large volume of serum for the military. The fulfilment of such demands must needs depend on the reserve of serum in stock. In fulfilling these demands interests of the civilian population for air raid protection shall always be safeguarded.

It is considered opportune and desirable that the expansion of the Calcutta Blood Bank during the war should be utilized to help develop greater post-war transfusion consciousness in both the medical profession and the public. With this end in view the Bank is taking the initiative with three steps—

1. To train doctors to take charge of a permanent transfusion service in their respective hospitals.
2. To encourage and help in the establishment of a panel of donors in all well-equipped hospitals in Calcutta and other parts of Bengal.
3. To supply serum for civil transfusion purposes to hospitals having a permanent Transfusion Unit. No discrimination shall be made in the use of such serums in these hospitals. If any discrimination is made the needs of the poor shall get preference.

CALCUTTA BLOOD BANK

We wish very urgently to draw the attention of the public to an institution which, we are sure, deserves the whole-hearted support of all citizens irrespective of their political or communal affiliation. It is the Calcutta Blood Bank whose business is to collect and supply blood and serum to meet the transfusion needs of all sections of the community.

We in this province have had not inconsiderable experience of air raids, and every time a raid occurs, we are reminded ever so much poignantly of the imperative need of a sufficient supply of bottled blood to save lives in jeopardy.

Political differences do not just enter into this matter. All political organizations recognize that when people suffer they must be rendered every help and protection. Total war of the sort to which we are getting accustomed brings in its wake recurrent hazards for the civilian population who therefore require special care and forethought.

We can unequivocally assure the public that the Blood Bank makes no discrimination between the needs of the civilian and the military population or between the Indian and European groups. We have been satisfied that the policy of the Blood Bank is always to safeguard the interest of the civilian population. Any individual or group of donors, again, may, if they so choose, designate in advance how they wish their donations to be utilized. This, to our mind, is a fair enough arrangement and should allay whatever misgivings may be in the public mind.

The Blood Bank proposes to try and develop greater post-war transfusion consciousness in both the medical profession and the public. Meanwhile, however, the exigencies of the war situation demand that our citizens should donate blood in much larger numbers than they have done so far, and that every well-equipped hospital should have its own stock of bottled blood for use during emergencies which are now so likely to occur.

Medical opinion is positive and unanimous that a normally healthy individual is never any the worse after donating his or her blood. We feel certain that in view of this assurance and in view of the fact that there can be few better ways of alleviating human suffering and of minimizing the death roll during emergencies than the gift of one's own blood to one's fellow citizens, our people should come forward, irrespective of their political affiliations, and help the Blood Bank in the most urgent, humanitarian task it has taken up.

1. Mr. Syed Badrudduja, Mayor of Calcutta.
2. Khwaja Sir Nazimuddin.
3. Mr. A. K. Fazlul Haq.
4. Mr. Kiran Sankar Roy.
5. Mr. J. C. Gupta.
6. Mr. A. R. Siddiqui.
7. Mr. G. D. Birla.
8. Mr. N. R. Sarker.
9. Sir Badridas Goenka.
10. Prof. M. N. Saha.
11. Mr. C. P. Lawson, M.L.A. (Central).
12. Mr. A. F. J. D'Mello.
13. Mr. Justice Amir Ali.
14. Prof. Hiren Mukherjee, President, Friends of Soviet Union.
15. Mr. D. P. Khaitan, M.L.A.
16. Dr. A. M. Malik, President, Indian Licentiate Medical Association.
17. Dr. P. K. Ghosh, Calcutta Medical Club.
18. Dr. A. K. Sen.
19. Dr. K. S. Ray, President, Bengal Civil Protection Committee.
20. Dr. B. C. Roy, Vice-Chancellor, Calcutta University.
21. Dr. Syama Prasad Mookerjee.

CORRIGENDUM

In the article by Dr. N. A. Purandare in our July number, on page 349, line 48, left hand column 'between the face positions' should read 'between the four positions'.

Public Health Section

THE HEALTH OF INDIA*

NUMBER 12 of the Oxford Pamphlets of Indian affairs is on the Health of India. This pamphlet, written by the Director of the All-India Institute of Hygiene and Public Health who is an American with a wide knowledge of public health in Asia, is an interesting and readable publication. We wish we could reprint the whole of this pamphlet in this journal. The pamphlet is already very condensed and in its 31 pages it covers a very wide field. It is difficult to give a true idea of the contents of this pamphlet and of the spirit in which it is written. An attempt to do is here made, but it is recommended that all interested in the subject—and these should include all educated persons in India—should purchase and read the pamphlet. We here quote certain portions of it and attempt to outline the portions which we cannot quote in full.

The pamphlet begins as follows :—

'The level of health in India is low. Preventable epidemic diseases such as smallpox, typhoid, dysenteries, cholera and malaria are widespread. Out of 6,165,234 deaths in 1939 malaria accounted for 1,411,614, smallpox for 48,103, cholera for 97,566 and dysenteries and diarrhoeas for 260,300. Tuberculosis is spreading and each year presents a more menacing problem. The resistance of the population to disease is low. Malnutrition and nutritional diseases are omnipresent. These in part account for the anemia which is particularly widespread among women and children. The heavy incidence of disease is reflected in the high mortality figures :

Comparative vital statistics for the year 1937 Indian and selected countries

	Death rate per 1,000 population	Birth rate per 1,000 population	Infant mortality per 1,000 births
India ..	22.4	34.5	162
Australia ..	9.4	17.4	38
U.S.A. ..	11.2	17.0	54
England-Wales ..	12.4	14.9	58
Ceylon ..	21.7	37.8	158
Java ..	18.8	28.3	106
Japan ..	17.0	30.6	106

'The low level of health is reflected in the expectation of life in British India which is stated to be 27 years, in contrast to an expectation of 67 years in Australia, of 63 years in England-Wales, of 63 years in Germany and of 47 years in Japan.

'In this pamphlet it is proposed to indicate the underlying causes of India's lack of health while giving an outline of the present public health and medical organization of the country.

'The health of a community depends on three factors : (1) The higher the standard of living the better the health. Machinery to assure living standards

adequate for the maintenance of health has to be provided. (2) The higher the standard of education the better the health. Teaching people how to keep healthy, how to prevent disease from attacking them and how to secure early diagnosis and treatment has to be an essential part of education. (3) An organized public health service to prevent disease and arrange for early diagnosis and early treatment.

'Each factor is essential and each supplements the others : it is difficult to dissociate their results. In India the standard of living is low and there is no social or economic machinery with which to level it up. Education is limited and poor in quality. At present some 88 per cent of the population is illiterate. So far only the third essential has been provided in some measure, and this service is still incomplete and still only in the initial stage.

'Adequate plans for public health service can be undertaken only with a knowledge of the realities of the economic situation. The results of any social service administration depend upon the money available and the way in which it is spent. Much ineffective administration results from violating this principle. It is obvious that there can be no results if a school medical service in India, with its annual *per capita* income of Rs. 65 (£5), is planned on the same administrative basis as in England—a country with an annual *per capita* income of £76 (1936) where the school medical service alone costs 7s. *per capita* of school population per annum. The economic problem must first be solved in India before there can be a significant school health programme. The solution lies in the development of a plan whereby the facilities purchased elsewhere at a cost of 7s. *per capita* can be obtained with the local economic resources. It can be done and has been done in other countries of relatively low economic standard. Limited funds do not make an adequate and good service impossible provided the people want the service and are prepared to contribute work in lieu of money, and provided there are people with the knowledge to plan such a service.'

The next section deals with social assurance and welfare.

'India's medical health policy, unfortunately, is still in the preliminary stage of being chiefly a disease policy. The latter is, of course, necessary and will continue to be, although becoming less necessary as it is recognized that disease is as much a result of social and economic maladjustments as of infections. . . . India almost entirely lacks effective social or economic measures for the maintenance of health.'

The pamphlet then discusses the recommendations of the Royal Commission on Labour, the provisions for workmen's compensation, and the maternity benefits for workers provided in six provinces. It is pointed out that

'Definite improvement in the health of the labour population will have to await implementation of many of the major recommendations of the Royal Commission. There is yet no provision for unemployment or pension insurance. Health insurance is under active consideration. In brief, social insurance in India is in its infancy. One may anticipate rapid growth in the coming two decades.'

'The Royal Commission on Labour (1931) made important recommendations to improve the present housing conditions. These included town-planning acts to provide housing for the working classes. Government, both central and provincial, have not as yet undertaken the solution of the problem in any significant manner, although small beginnings have been made in the larger metropolitan cities and in Delhi province.

*The Health of India. By J. B. Grant. Published by the Oxford University Press, Humphrey Milford. Available from the Oxford University Press, Bombay and Calcutta. Price, As. 4.

The Labour Commission also appreciated the importance of nutrition in improving the health of workers. As yet, however, little of significance has been effected in this field so essential for the maintenance of health and prevention of disease.

'With a purchasing capacity of only about 2½ annas a day, the average Indian is only able to meet his energy requirements with cheap carbohydrate foods like rice and cannot afford sufficient protective foods. Deficiencies in diet such as animal protein, calcium and vitamins A and C are widespread. The result is poor physique, high maternal and infantile mortality rates and a low expectation of life.'

'The relatively little space given to discussing social welfare measures for the maintenance of health in India merely reflects their absence and not their unimportance.'

The next section of the pamphlet deals with health education and says:

'Health instruction in primary and secondary education cannot develop beyond the general level of education, which in India is very limited, as reflected in the illiteracy rate of 88 per cent. . . . General education being what it is one can hardly expect health education in India to be regarded as of any significance, and until this defect is corrected India's health will not improve.'

The report then quotes the recommendations of the Central Advisory Board of Health on adequate health instruction in India.

The next section of the pamphlet deals with public health and outlines the history of the public health services. It points out how the Government of India Act of 1918 transferred the responsibility for local and medical health administration to the provincial governments and states:

'Although there has been quantitative expansion of public health activity in the provinces since 1921, the quality of work suffers from the weak control of the local governments over the local bodies. . . . Prior to the 1919 Reforms local self-government in India was of the continental, highly centralized type. The Act of 1919 decentralized local self-government before experienced traditions and public opinion had had time to develop. . . . Education has not so far advanced sufficiently to hold out promise of immediate efficient local government in the social welfare fields. In the interim it was unwise so completely to relinquish the provincial governments' control over local bodies to the extent seen particularly in Bengal; and it might be wise for governments to centralize the welfare services for a given period.'

The next section deals with central organization and ends with a paragraph on the Central Advisory Board of Health constituted in 1937:

'The Central Advisory Board of Health constituted in 1937 has great potentialities for planning, so essential to effective health protection. Although restricted to an advisory capacity, it has stimulated the development of specific provincial organs for dealing with nutrition, malaria and school health. The board is representative not only of the provinces, but also of the Indian States. The Public Health Commissioner is the Secretary of the Board. It provides the nucleus from which will evolve the federal administration that will eventually prove essential.'

Provincial organization is then discussed and it is stated that in its earlier phases

'The objective was largely control of epidemics, particularly cholera, smallpox and plague. A fourth stage is now emerging with the addition to the centralized (horizontal) administration of specific vertical

functional organizations, particularly for malaria, maternity and child welfare, nutrition, and—very shortly—for school health. The stage of evolution varies in the individual provinces but is along the same lines. The provincial public health departments are mainly concerned with rural public health.'

Under 'rural health administration' the following remarks are made:—

'The Bengal organization is comparable to that of other provinces. The present average peripheral unit is a health circle around 80,000 of population and 80 square miles. This unit has come into existence only during the past decade and a half. Its establishment was also primarily for the purpose of controlling epidemics, especially smallpox and cholera, and for prevention of adulteration of food. The staff consists generally of a sanitary inspector, assisted by one health assistant, one or more vaccinators and a medicine carrier. The whole cost (Rs. 12 lacs in Bengal) is borne by the government on condition that the district boards should not reduce their expenditure on public health.

'There are altogether 6,500 curative dispensaries and hospitals in India, which can treat annually only a total of 35 million new and old patients. The bulk of medical relief for India's 400 millions, of whom more than 80 per cent live in villages, is still provided through the indigenous pre-scientific systems of medicine and their practitioners. It cannot be otherwise with the relatively small provision of modern service. Each district is provided with at least one hospital under a civil surgeon, with or without hospitals at sub-divisional headquarters under assistant surgeons. Bengal has 217 hospitals with 6,189 beds, in addition to 1,214 dispensaries which are staffed by 460 medical officers and 1,819 sub-assistant surgeons. The hospitals and dispensaries are in general supported by the district boards or union boards. Generally in the first instance the hospital or building in question is the gift of some citizen.

'The district public health and medical expenditure is usually subsidized by the government and local bodies to approximately 60 per cent. Theoretically the government grant-in-aid carries the right to nominate and to remove health and medical officers. In reality this power rests with the district board.

'The foregoing outlines the basic organization. Before proceeding further it is necessary to examine the achievements of this basic organization, particularly in the field of public health. These cannot be considered good in comparison with results in other Asiatic countries if continued heavy smallpox and cholera are the criteria.

'The relatively poor result in India has not been due to either lack of funds or personnel. Bengal has 3,018 vaccinators and spent Rs. 4,70,644 in 1940 specifically to control smallpox. One important reason for this poor result undoubtedly has been the greater decentralization of local self-government in India than in other countries. Decentralization before the level of technical public opinion in local bodies has reached a certain stage is dangerous.

'The most acute problem in India at present is that of bringing medical protection to the individual villager who has hitherto been largely neglected. Its urgency has, as might be expected, resulted in varying viewpoints as to its solution. Two chief trends are observable during the past decade. On the one hand there is the policy inaugurated in Madras in 1925 of subsidizing rural practitioners with Rs. 50 a month to induce them to live in the mofussil. It was carried one step further in 1934 by the payment of an additional subsidy of Rs. 15 per month to practitioners who after a short course of training would discharge certain public health functions. Results to date have not been good. The other trend, exemplified best in the Punjab, is to combine curative and preventive functions at the periphery, and to add public health to the curative responsibilities of the dispensary physician. This was inaugurated in 1938. . . .

'The unification of curative and preventive functions under a single administration is essential and has become an axiom in public health. This is particularly so in India, and Major-General Sir John Megaw, late Director-General, Indian Medical Service, pointed out that "it is impracticable to draw a sharp line of distinction between medical relief and disease prevention. The ideal to be aimed at is to have effective co-operation between the workers who are engaged in these two forms of medical activity. Division of labour is desirable and even essential in certain matters but when we come down to the small units, such as village dispensaries, India cannot afford to maintain two experts in each centre of population. There is no reason why the dispensary doctor should not assume responsibility for the general supervision of the health of the area in which he works."

Under urban health administration the following statements are made :—

'According to available information, nearly half the districts and three-quarters of the municipalities in British India still are without qualified health officers. . . . Under the existing local self-government acts municipal councils have been given almost complete responsibility for public health, but in many of the areas visited by us we were unfavourably impressed with the standard of health administration and with the manner in which these duties have been performed. Health officers are to be found in most of the larger municipalities, but their work is too often ineffective because they have incomplete control of the health organizations or because their recommendations fail to receive active consideration from their councils. In the first place, only a minority have so far appointed qualified health officers, and this defect should be remedied at the earliest possible opportunity, whilst municipal health organizations should also be improved and strengthened. Secondly, all by-laws and regulations dealing with health, housing and sanitation should be revised and brought up to date. Under the existing law the duty is given to municipal councils of framing by-laws on such matters, but instances are not wanting where these have never been prepared, and efficient enforcement of those in existence has rarely been practised.

'The level of health organization in Bengal is indicated by the fact that of the 116 second-class municipalities only 27 are provided with full-time medical officers of health. Twenty-eight do not have a sanitary inspector, while eleven do not have even a vaccinator, who is generally the first type of public health officer to be employed.

'A defect is the absence of boards of health competent to provide technical advice. The health committees of the corporations are political bodies changing annually and selected from the councillors, most of whom have not had previous opportunity of considering public health or medical question.'

The pamphlet then discusses medical education. After briefly outlining the history of medical education in India the report states :

'A lower standard of medical qualification has proved an interim necessity in the evolution of medical education throughout the world. It is, however, a temporary phenomenon resulting eventually in the lower standard being raised to a university level or the school in question being abolished. This stage is now being reached in India and is expected to close in another quarter of a century. . . . The range between the best and the worst medical schools is very wide.'

Under medical registration the following statements are made :—

'There are approximately 42,000 doctors, of whom two-thirds are licentiates. This total is less than Japan's for a population approximately the same as

Bengal's. If there were one physician per 2,000 of population, India would require 200,000 doctors.

'The first provincial medical council was established in Bombay in 1912, since when councils have been established in all the provinces. The function of the provincial councils is to regulate the practice of scientific medicine without, however, interfering with the indigenous systems.'

The pamphlet then discusses nursing, opening with the statement :

'There are less than 4,500 nurses throughout the country as compared with 42,000 doctors, and this is a measure of the present backward status of the profession.'

Details are then given of the organization of the nursing profession, and the need is emphasized for a larger number of nurses, for better nursing facilities, for specialist training after qualification.

Health visitors are then discussed :

'The emphasis of health visiting in India is on maternity and child welfare. Students must first qualify as midwives before undertaking their 18 months' training in the health visitors' schools. Practice in the latter, to all intents and purposes, is limited to maternity and child welfare. Even in this single field of early diagnosis and preventive treatment of disease the demand for visitors far exceeds the supply. Only 350 of the 828 welfare centres were provided with certified visitors in 1938. Public health nursing is as yet unknown in India. Until this comes into being there cannot be modern administrative services for the other fields of early diagnosis and preventive treatment, particularly school, industrial tuberculosis and venereal disease services.'

In the section on industrial health the following remarks appear :—

'Industrial health is still chiefly a private responsibility and can scarcely be said to have become a major activity. There has been no significant improvement since the recommendations of the Royal Commission on Labour in India (1931), whose two chapters on Health and Housing for the industrial worker give a detailed description of the present situation. . . .

'A very considerable medical service is provided by the larger industrial concerns, but these are mainly concerned with medical relief and ordinary public health measures of prevention, such as anti-malaria work. . . .

'The inauguration of an industrial health policy and programme is long overdue on the part of both central and provincial governments.'

The pamphlet ends with a section of conclusions outlining the need for consolidated health acts, for the adoption of sound principles of health administration, for planning a definite programme of co-ordinated health work and for demonstrations of such plans, for improved training of doctors and nurses, and a great increase in the numbers of nurses trained.

These abstracts from an interesting pamphlet are mostly devoted to criticism of the present situation, but it would be wrong to get the idea that the pamphlet is entirely devoted to finding fault, for it makes many constructive proposals and it contains a mass of information which will be most useful to those who will try to plan and carry out the greater development of health work in India which the author of this pamphlet believes will be seen within the coming years.

Current Topics

Treatment of Chronic Ulcerative Colitis by Pneumoperitoneum

By H. NEUMANN, M.D.

(From the *British Medical Journal*, Vol. I, 2nd January, 1943, p. 9)

In many cases of chronic ulcerative colitis conservative medical treatment is ineffective. A considerable number of drugs are usually tried, and patients are kept in bed for months under strict diet and daily irrigations. Some recover after prolonged treatment, others find temporary relief, but there are always cases which seem intractable. Sufferers from this not rare disease frequently belong to the intelligentsia between the ages of 20 and 30, and as even milder forms with 8 or 10 daily bowel motions make them unsociable and unfit for work, drastic therapeutic methods have been employed.

Many writers are in favour of extensive colon resection, and H. W. Cave of New York proposes subtotal colectomy as the method of choice. He believes that the percentage of lasting cures is so small that colectomy is a measure of necessity. On the contrary, we have obtained excellent results in chronic, apparently intractable, cases with a far less drastic and dangerous method—the establishment of a therapeutic pneumoperitoneum and its maintenance over several months. With this measure the patient is not confined to bed except for the first few days, and his sojourn at the hospital can be limited to a short time. Indications for pneumoperitoneum were made on clinical grounds—perchloricity, diarrhoea, pus, mucus, blood in stools, intractability—and little weight was put on bacteriological findings, as various organisms caused clinically indistinguishable forms.

TECHNIQUE OF PNEUMOPERITONEUM

The technique is simple, and can be carried out by any practitioner. The therapeutic pneumoperitoneum may be installed with any model of the usual pneumothorax apparatus and with the same needles as are used for the pneumothorax—the most suitable being fairly thin ones with closed, wedge-shaped, not very pointed end and lateral opening, and a diameter of about 1/25 inch or less. Using such needles, local anaesthesia is not required. The best place to puncture is about an inch to the left of and below the umbilicus. After painting the skin with iodine, and examining the needle for free passage of air, the skin is well stretched between two fingers to give resistance to the needle, which, still in connection with the manometer of the pneumothorax apparatus, is pushed through skin and abdominal wall. After short practice it is not difficult to distinguish, from the resistance to the needle, the layers of the abdominal wall, and particularly the piercing of the peritoneum. This moment is rather more painful than when the pleura is pierced, but with sufficiently thin needles I have never found it necessary to use novocain, which would make it more difficult to distinguish the abdominal strata. It also seems that the patient soon becomes accustomed to the pain of the piercing of the peritoneum, and after several refillings it is felt but little.

It is more important than with pneumothorax to feel the strata at the progress of the needle, as of course the manometer gives no indication whether the needle has passed the peritoneum. The danger of piercing the bowels seems very remote: the smooth intestines escape the needle if they are not too tympanitic and if the needle is not too pointed. Also, with the finer needle there would be no danger if the bowels were pierced.

Before passing air through the needle it is advisable to test with a stylet whether blood or any liquid is

present. The amount of gas introduced averages 500 c.cm.—oxygen or air being used. The reading at the manometer is round about zero, rising slightly after the filling of each fraction and dropping again quickly, eventually remaining at 2 or 3 cm. H₂O. Sometimes slight oscillations corresponding to the respiration are noticeable. If the needle has not yet reached the peritoneal cavity the manometric pressure of course rises rapidly, even after introducing the smallest amount of gas. The manometer serves in this sense as a control.

Another control is the reduction and the disappearance of the dull liver sound on percussion. During or soon after the filling, the patient usually complains about the sudden appearance of pain in one or both shoulders; this is of so regular occurrence that it is advisable to tell the patient beforehand about it and to reassure him. The appearance of this phenomenon and the projection of pain to the shoulder region are obviously due to the phrenic nerve, and can also be used as a control; the effectiveness of the filling can further be checked by means of radiographs.

Refilling can be done once or twice weekly; when pure oxygen is used the intervals are 3 or 4 days because of more rapid absorption. When air is used the intervals are from 6 to 8 days. Because of its calming effect oxygen is preferable for the first fillings—for cases with major abdominal discomfort and frequent colics, and for cases with a higher grade of secondary anaemia and dyspnoea. The number of fillings required varies greatly, and it may be necessary to continue treatment for 3 months or more.

RESULTS

Of the 7 cases in the series only one was treated for more than 3 months.

Case 1.—A woman, aged 28, had been suffering for 3 years from severe diarrhoea. She had from 15 to 25 bowel motions daily—in better periods and under the influence of opium 10 to 12 motions—always with an admixture of mucus and blood, occasionally pus. Loss of weight was 46 lb. in 3 years. During 3 months' treatment with pneumoperitoneum the number of bowel motions was steadily reduced and she regained 17 lb. Her general condition improved, and finally the stool was free from mucus and blood. The diagnosis of ulcerative colitis had been confirmed by sigmoidoscopy. Investigation after one year showed that she was free from complaints and had further gained in weight.

In one case only two fillings were required. Particulars of this case are as follows:

Case 2.—A man, part Polynesian, aged 42, had been suffering from symptoms of chronic colitis for several years. His loss of weight was over 30 lb. and there was incapacity for work and general debility. After pneumoperitoneum and one refilling he felt well. No sigmoidoscopy had been carried out; the presence of a tumour in the colon suggested by severe secondary anaemia had been excluded by radiological examination. Re-examination after 7 months showed that the patient had gained 14 lb. He was still feeling well and was able to work.

In some cases a moderate amount of peritoneal effusion developed; this liquid was sooner or later reabsorbed spontaneously. In such cases it is advisable to give 10 c.cm. of calcium chloride intravenously 3 times weekly. It appeared also that patients who developed temporary ascites responded more quickly to treatment.

SUMMARY

The therapeutic action of pneumoperitoneum is probably due partly to activating the visceral peritoneum and 'tuning it to a higher pitch' by the setting up of a permanent bland irritation to the vast peritoneal surface, and partly to mechanical action and indirect influence on the autonomic nervous system.

Pneumoperitoneum may be described as a simple and effective therapeutic procedure in apparently intractable cases of chronic ulcerative colitis. It is easily performed, and is free enough from danger for

it to be introduced, and for refillings to be made, by any practitioner, even without the facilities of a clinic or a hospital.

Observations on Naturally and Artificially Induced Quartan Malaria

By M. F. BOYD

(*American Journal of Tropical Medicine*, Vol. XX, November 1940, No. 6, pp. 749-798)

THIS paper contains a very comprehensive analysis of observations made on forty-three patients subjected to malaria therapy with *P. malariae*. Three strains of the parasite were used; they came from widely separated localities but no observations were made to determine their antigenic relationship. In five patients infection was naturally induced; in forty-three patients trophozoites were inoculated, intravenously. In naturally inoculated cases the incubation period varied between four and five weeks; parasites were detected in the blood from three to twelve days before the clinical onset. In artificially induced infections the mean interval between inoculation and the first detection of parasites was 9.5 days, and between inoculation and the clinical onset 19.2 days. The mean duration of naturally induced attacks, regardless of therapeutic interference, was 132 days, and of artificially induced attacks 92 days. Early paroxysms were always simple quartan in type; double quartans and quotidian fevers were seen only in advanced stages of the attack. An onset with remittent fever was rarely seen. Paroxysms after artificial inoculation show greater complexity and irregularity than those following natural infections. The parasite densities observed were considerably lower than those commonly observed in *P. falciparum* and *P. vivax* infections. In one very exceptional case of the series, however, a parasite density as high as 114,000 per c.mm. was observed on one occasion; this patient died, apparently of malaria, in spite of heavy doses of quinine. In the two other cases that terminated fatally malaria does not appear to have been responsible for death.

But little justice can be done to this exhaustive study within the scope of a summary.

Reprinted from the '*Tropical Diseases Bulletin*', Vol. XXXVIII, No. 7, 1941.

Skin Diseases in War

By R. T. BRAIN, M.D., F.R.C.P.

(From the *British Medical Journal*, Vol. II, 26th December, 1942, p. 760)

THE various infections of the skin account for the great majority of skin diseases in war, and these infections may be considered conveniently in their aetiological groups. Thus we have the common pyogenic infections, seborrhæic dermatitis, mycotic infections, virus infections, and those due to animal parasites. In many of these conditions the diagnosis is simple and calls for little comment, while treatment is of supreme importance not only to the individual but to the community, for the speedy cure of an infection is the most certain method of preventing its spread.

THE PYOGENIC INFECTIONS

The common infections to be considered under this heading are of streptococcal or staphylococcal origin, but it should be remembered that mycotic and virus lesions, and also the less familiar lesions of cutaneous diphtheria and leishmaniasis, may be pustular too.

IMPETIGO CONTAGIOSA

Several clinical varieties can be recognized, the discrete scabbed sore being the most common. Bullous lesions suggest greater virulence, and the spread is usually rapid. As the bullæ resolve rupture by drying centrally, the edges remain red and may extend as a

circinate lesion closely resembling tinea but more rapid in its course. Rarely, ulcerative lesions termed 'ecthyma' occur, and this variety leaves scars. Occasionally pale scaly lesions—impetigo pityroides—are present with or without the other varieties, and such lesions are apt to be confused with the scaly seborrhoids, to which they are probably related. Impetigo often involves the angles of the mouth, producing septic fissures; it also attacks the skin folds, setting up a septic intertrigo, the post-auricular variety being the most common. Septic fissures and pus-coecal intertrigo are likely to persist as chronic lesions long after the primary condition of impetigo has cleared up. Sometimes in the course of impetigo, either because the infection is very acute or the skin is irritated by treatment, a rapidly spreading pus-coecal dermatitis results. This appears as a bright erythematous area—hot, slightly oedematous, often weeping or crusted, but not indurated or so well defined as erysipelas, and the constitutional disturbance is lacking. A weeping pus-coecal dermatitis is often loosely called 'eczema', but it is advantageous to retain the latter term for the response of a hypersensitive skin in which grouped minute papulo-vesicles erupt in non-inflamed areas. Naturally a skin may be sensitized by an infection or by an irritating application, and then upon the dermatitis so produced the grouped eczematous lesions will appear; but if the eczematous nature of the new eruption is not at once apparent by its morphology it soon will be when further 'eczematous' lesions arise outside the inflamed area and perhaps symmetrically upon the limbs. The distinction between dermatitis and eczema is of practical importance because in acute pus-coecal dermatitis the infection must be fought, whereas eczema calls for sedatives and emollients to soothe and desensitize the skin.

Before discussing treatment it is necessary to add that few dermatologists claim to be able to distinguish between staphylococcal and streptococcal lesions of impetigo contagiosa. Streptococci have often been found in pure culture in early bullous lesions, which cannot therefore be regarded as peculiar to impetigo of staphylococcal origin. The dramatic response of many cases of bullous impetigo to a sulphonamide adds support to this view.

TREATMENT OF IMPETIGO

One might say provocatively that general treatment is unimportant, for most of the cases clear up quickly on local treatment alone. Even so, it is bad practice to treat any lesion and neglect the individual, and in the exceptional case general treatment is vital: this happens when a virulent organism or lack of resistance on the part of the patient produces a rapidly spreading infection, the lesions of which are deeply coloured with an erythematous flare spreading around them like a developing erysipelas. Sulphanilamide is usually quickly effective in such cases, doses of 1 g. three or four times a day for a week being adequate as a rule. Although such relatively small doses rarely produce toxic symptoms, ascorbic acid is a safeguard, and as wartime diets are low in vitamin C content, doses of 50 mg. two or three times a day are useful. Personal experience and reported cases suggest that vitamin C is very helpful in many infections, so that it is worth while giving it alone in obstinate cases of impetigo. Chronic pus-coecal lesions such as septic fissures and intertrigo may resist local treatment for years unless every effort is made to improve the general health. The good effects of ultra-violet light upon immunity and metabolism should be considered. Phenobarbitone has cured many an obstinate case of impetigo in a nervous subject whose picking at the sores, even during sleep, has frustrated local treatment.

Local treatment is determined by local conditions. The most important fact to remember is that the normal dry intact horny layer is invulnerable to bacterial infection. A moist skin is a vulnerable skin, so that the indiscriminate use of water or grease is to be avoided. The exudate from moist pus-coecal lesions can permeate the stratum corneum, thus bringing the

organisms in a suitable culture medium to the moist layers, where they may actively infect; and no doubt this explains the spread of bullous impetigo on the face by a pillow at night. This can be prevented by soaking a clean handkerchief in liq. hydrarg. perchlor., pinning it when dry to the pillow, and lightly powdering it with talc. Auto-infection by scratching can be diminished by cutting the nails short, scrubbing the free edges, and disinfecting them with antiseptic—an important fragment of technique in nervous patients and in children. Obviously it is equally important to dry up the early lesions as soon as possible. When these lesions tend to dry and heal spontaneously it is sufficient to apply calamine lotion or a dusting powder, and cure may be expected in a few days. Flat scabs on dry lesions may be left undisturbed and in due course they will flake off the healed skin, but the scabs on purulent sores need removing so that the antiseptics may inhibit or destroy the infection. A simple and satisfactory method of removing scabs and crusts is to apply hot compresses of 2 per cent sodium sulphate for one hour and then to cleanse with a similar lotion or with 1 per cent solution of sodium bicarbonate or normal saline. Dettol, hydrogen peroxide, or hypochlorite solution may usefully be added to the cleansing lotions. The need for isotonic or slightly hypertonic solutions is stressed, because skin denuded of its protective stratum corneum is instantly damaged by water, and the H-substance released by the disrupted cells increases the erythema and exudation. The starch poultice brings heat and moisture into more intimate contact with the skin, but it is less cleanly than the saline compress. Kaolin made into a paste with 2 per cent sodium sulphate solution is a simple substitute for the starch compress.

Having cleaned away scabs and exudate, the next object of treatment is to dry the moist surface. Local ultra-violet light is an excellent method if available, since this has a superficial bactericidal effect and also stimulates healing and increases the resistance of the skin. Failing ultra-violet, infra-red or the near light of an electric bulb, or the warm air of an electric dryer can be used. In actual practice one often has to depend upon powders and drying lotions. As a powder basis, zinc oxide, talc, and kaolin should be used instead of starch, and 2 per cent of ammoniated mercury or calomel or 5 per cent of sulphanilamide may be incorporated. Sulphanilamide powder alone is effective in the treatment of virulent lesions but more active as a 5 per cent solution in glycerin.

In mild infections calamine lotion alone or with 2 per cent liquor picis carbonis or 0.1 per cent mercury perchloride is to be preferred as a cosmetic application. A suitably tinted 20 per cent suspension of kaolin with 0.1 per cent mercury perchloride or 2 per cent ammoniated mercury is a useful alternative. If these lotions do not control the exudate—and occasionally metallic substances increase it—the dyes should be used. A 2 per cent watery solution of gentian violet is excellent, although it obscures the lesion more than 0.1 per cent acriflavine, to which 4 per cent of tannic acid may be added to coagulate the serous discharge. Certain metallic salts also have a coagulating effect; useful formulæ being silver nitrate 2 to 5 per cent in distilled water; or eau d'Alibour, zinc sulphate gr. 6, copper sulphate gr. 4, in 1 oz. of water. Alcoholic solutions irritate the broken skin, and even spirit soap is best avoided.

If the skin becomes too dry or if eczematous lesions indicate intolerance of watery applications, creams or pastes should be tried. The former consist of 6 to 10 per cent of calamine or of zinc oxide in a mixture of a vegetable oil and an equal volume of lime-water. Up to 10 per cent of lanolin may be added to make a smoother cream, and the further addition of 2 per cent of ichthammol, phenol, or liquor picis carbonis serves to relieve irritation and to add an antiseptic quality to the cream.

Zinc paste consists of one part of starch, one of zinc oxide, and two of soft paraffin. No doubt it would be just as effective if made with equal parts of kaolin

and vaseline. These pastes may be improved for certain conditions by adding 2 to 3 per cent of crude coal tar or of yellow oxide of mercury. Either may suit a dry impetigo, an obstinate intertrigo, or an eczematous lesion intolerant of lotions. Since pastes contain 50 per cent of powder they can absorb moisture from the skin, and their degree of permeability prevents maceration and overheating. Compared with ointments, pastes represent a saving of nearly 50 per cent of the fatty base—an important economy in war.

Ointments have a limited sphere of usefulness, and their irrational employment on moist lesions accounts for a lot of unnecessary dermatological practice. The skin is kept moist and vulnerable to infection under greasy films, and the formation of a healthy stratum corneum is retarded because desiccation is part of its natural stimulus. It is true that, according to many textbooks, ointments have a prominent place in the treatment of impetigo, ung. hydrarg. ammon. being popular in this country and the U.S.A. and diachylon ointment in some European countries. It may fairly be said that many cases of impetigo get well in spite of the use of ointments, and that with careful cleansing of the lesions before applying ointment successful results can usually be obtained, although it may entail daily visits to a clinic. The advantages of substituting lotions for ointments can readily be demonstrated. A weak mercurial ointment is useful when hard scabs form at night, especially in the scalp, and ung. hydrarg. nitratis dil. often heals septic fissures which are apt to persist at the angles of the mouth and just inside the alae nasi. Quinolol ointment and the sulphanilamide ointments are sometimes more effective than the mercurials, but they are rarely necessary in the treatment of impetigo.

Some patients are very susceptible to staphylococcal infection of the hair and sebaceous follicles, and since grease increases this susceptibility sycosis barbae may be a sequel to treating impetigo of the beard area with an irritating ointment.

both may do good; but often, although specific antibodies in circulation may be increased many-fold, the skin susceptibility to infection persists, and so does the sycosis.

SEBORRHOIC DERMATITIS

Seborrhœic lesions are common and troublesome in war for reasons not difficult to understand. Whatever is the true nature of these conditions—and that remains controversial—the importance of constitutional factors is generally accepted. The subjects may be plump and placid or thin and nervous, but both types have moist greasy skins, have generally a liking for carbohydrates, and are always very prone to infections of their skins and mucous membranes. Nervous and anxiety states, limitation of protein and of protective foods, and restricted facilities for personal hygiene are the aggravating factors of war. The indications for general treatment therefore are clear, and it remains to consider the local conditions.

The indisputable seborrhœic lesion is the pale pink macule which occurs on a scurfy scalp and tends to spread behind the ears and to the margins of the scalp, the midlines of the back and chest, and the folds and flexural surfaces. These lesions of seborrhœic dermatitis are large confluent patches or discrete macules, circular, oval, or circinate in pattern, the latter suggestive of *tinea circinata*. The colour is a very pale pink as a rule; the lesions are irregularly covered with a soft, greasy, flaky scale, and irritation is slight or absent. Follicular papules topped by a small scale may be present on the greasy skin too, and acne vulgaris is common in the young seborrhœic patient and rosacea in the middle-aged. This tendency to follicular lesions is further marked by a frequency of boils, indicating a characteristic susceptibility to staphylococci which probably accounts for many seborrhœic lesions. The importance of the *pityrosporon* of Malassez, the organism predominant in scurf, remains doubtful, therefore, in spite of the fact that treatment of the scurfy scalp is the keystone of local therapy. For this purpose ointments of sulphur, salicylic acid, or resorcin are used to soften and remove the scales, the process being completed by a shampoo, using a 2 per cent solution of sodium bicarbonate and a tablet of sulphur or carbolic soap. Spirit soap is very effective, but is more likely to irritate an inflamed scalp. A liniment of 5 per cent salicylic acid in 1 part of spirit and 7 parts of castor oil, a cream of 2 per cent ichthammol in *lotio calaminæ oleosa*, and a lotion of 2 per cent precipitated sulphur in calamine lotion are very useful for seborrhœic lesions of the scalp and skin, while many of the remedies and methods used in the treatment of impetigo can be advantageously employed.

MYCOTIC INFECTIONS

The epidermophyton infections are by far the most common variety in war, and, since the feet are the usual sites involved, early diagnosis and effective treatment are essential. The former is usually simple, for an erosive dermatitis spreads from the toe clefts to the sole of the foot, with a circinate advancing edge of itching pustules or vesicles. The horny layer, separated by exudation, breaks and peels off, leaving moist red tender areas. Distant groups of tense vesicles may arise in the middle of the sole, and sometimes the infection begins here. A scraping of the under surface of a vesicle mounted in 10 per cent sodium hydroxide may reveal the fungus and confirm the diagnosis of *tinea pedis*.

Unfortunately, epidermophyton readily sensitizes the skin so that deep vesicles erupt on the soles and also on the palms, and in these vesicles no fungus can be demonstrated; nor do the lesions respond to fungicides, but usually they do resolve when the primary mycotic infection is cured. These allergic eruptions, called 'epidermophytids,' are clinically indistinguishable from the eczematous conditions of podo- and cheiropompholyx, which, like other types of eczema, clear up and tend to recur without any obvious external cause. *Tinea* relapses because of residual infection, often

apparent in the fourth toe cleft as thick white cuticle, speckled at the sites of small vesicles. Eczematous lesions must not be treated with strong antiseptics or fungicides; hence the importance of recognizing them so that general and local sedative measures may be employed.

Pyogenic intertrigo of the toe clefts is often confused with *tinea*, but the septic process is more acute, the surface moist at the sites of ruptured bullæ, and as a rule the infection spreads to the more delicate dorsal surfaces of the toes. Scabies may be the cause of vesicles and pustules on the feet, and from the infected lesions an extending pyogenic dermatitis sometimes resembles *tinea*. More rarely, pustular psoriasis or acrodermatitis perstans has to be distinguished from *tinea*, for in these conditions, clinically identical, groups of pustules erupt in the middle of the soles. These pustules are generally set in dry shiny red plaques suggestive of psoriasis; the contents are usually sterile, and treatment with fungicides is ineffective.

Epidermophyton infection of the groin—*tinea cruris*—is either secondary to *tinea pedis* or is acquired from infected lavatory seats or clothing and towels. As in the case of scabies and pediculosis pubis, *tinea cruris* may be a venereal contagion. The disease begins as small scaly pink macules, resolving in the centre and spreading centrifugally with a scaly edge so that by the time advice is sought the lesions are already circinate and the diagnosis rarely in doubt. *Monilia* infections are so similar that they are diagnosed as *tinea*; but this does not matter, because they respond to the same treatment. On the other hand, intertrigo when mistaken for ringworm is likely to be irritated by treatment with fungicides, and indeed this common lesion of the groin may be a sequel to the treatment of *tinea cruris*.

Intertrigo begins in the depth of a fold, as a bright erythematous patch, fading towards the edges—in contrast with the ringworm lesion. The friction of coarse woollen clothing on a moist skin often produces intertrigo of the inner sides of the thighs near or adjacent to the scrotum, and because of this location a diagnosis of *tinea* is apt to be made. Either of the lesions may be found in the axillæ too.

TREATMENT OF EPIDERMOPHYTON INFECTIONS

The crural and axillary lesions will clear up in a week or two if treated efficiently, and a simple method is to use Whitfield's ointment—ung. acid. benzoic. co., B.P.C.—a little well rubbed in at night, and, after cleansing with soap and water in the morning, to apply a mild antiseptic lotion. The dilute mercurial ointments will also cure early infections, and when necessary the fungicidal effect can be enhanced by adding 4 per cent of chrysarobin or 0.5 per cent of derobin or cignolin. The sole use of such ointments will cure many cases of *tinea cruris*; but there is less chance of producing a dermatitis and the skin is more comfortable if kept dry with a lotion by day. Underclothing must be disinfected. *Tinea pedis* should be treated on similar lines. The strong ointments are well tolerated, and 4 per cent of tannic acid in acriflavine lotion is useful to control hyperhidrosis. Relapses are common because the fungus is protected from therapeutic agents by the thick horny layer of the sole, which is often greatly hypertrophied at the sites of infection. The trichophyton is even more inaccessible if it reaches the nail folds or under the nail-plate, where it may give rise to onychomycosis. So after an apparent cure it is important to prescribe a spirit paint for use after washing the feet. A suitable one is 0.2 per cent of mercury perchloride and 2 per cent of salicylic acid in surgical spirit; this should be painted around the nails and in the toe clefts for at least six months. Its use on the soles of the feet would be a good prophylactic measure. Socks must be disinfected and the insides of boots treated with formalin.

Trichophyton infections, and occasionally microsporon infections, account for *tinea circinata*, the common ringworm of the glabrous skin. Diagnosis is easy as a rule,

and the treatment is that given for tinea cruris. The pustular ringworms give more trouble, and tinea barbae is not infrequently confused with sycosis barbae. Ringworm of the beard area presents an indurated granulomatous swelling studded with pustules. These may show a circinate pattern and thus give a clue to the diagnosis, which may be confirmed with some difficulty by pulling a hair out of a pustule and mounting it, and the pus with it, in 10 per cent sodium hydroxide. Fungus or spores may be seen with the 1/6-in. objective under restricted illumination. The usual treatment of tinea can be applied to tinea barbae, but the hairs should be epilated from the pustular follicles. Hot compresses of 5 per cent sodium thiosulphate or of 10 per cent lotio calcei sulphurati are often helpful. Large doses of sodium iodide should be tried in deep and obstinate mycotic infection.

VIRUS INFECTIONS

Herpes simplex most commonly occurs on the face, where it is often mistaken for impetigo. The sudden eruption of grouped vesicles on an inflamed base with preceding irritation is the clue to the diagnosis. Penile herpes is not uncommon, and must be distinguished from scabies and primary syphilis.

Zoster presents similar herpetic lesions, and when seen late in a confluent pustular stage the resemblance to impetigo is close. The sharply unilateral distribution and the rapid evolution of the full eruption establish the diagnosis, and a history of preceding pain or hyperaesthesia completes the clinical picture. If pain is severe hypodermic injections of 1 c.cm. of pituitrin, or sodium iodide in doses of 15 to 20 gr. t.i.d., may give relief. Herpetic lesions of both types are best treated with 1 per cent phenol in calamine lotion.

Warts may be just unsightly or, owing to their situation, may be the cause of disability. In either case they are a virus infection, and so are likely to spread on the individual or to infect others. Treatment, especially of the solitary wart, is a much-neglected but important fragment of preventive medicine. When warts are few in number their complete removal or destruction should be attempted. Curettage with a sharp spoon and subsequent sterilization of the crater with pure phenol is often satisfactory. Cauterization by heat or with CO₂ snow has the advantage of leaving a dry surface, and after diathermy or galvano-cautery no dressing is required. These methods appear to be radical and certain, but they are not; for the virus may be distributed more widely than the lesion indicates, and under the stimulus of the virus the interpapillary processes of the epidermis thrust deeply into the corium. The epidermal cells carry the virus with them, so that a single surviving cell presumably can account for a recurrence of the wart. Fortunately many warts disappear if they become involved in an inflammatory reaction, however slight, and this probably accounts for the successful use of x-ray therapy and of ionization, although considerable evidence exists of a favourable response to suggestion, which is unseparable from impressive techniques. When warts are numerous caustic paints should be used; but it is essential to pare away the thick horny cap continually, because it is resistant to most of the preparations that may safely be entrusted to the patient. Salicylic acid is a safe and effective keratolytic, and a 10 per cent solution in collodion or spirit forms the basis of many paints for warts.

Painting is more effective if the wart is kept covered by adhesive plaster, and a resistant plantar wart may respond to this method if painted every other day with liquid phenol or 80 per cent trichloroacetic acid in water. After several painting the thick horny cap often comes away adhering to the plaster, leaving a deep crater, which should be again painted with phenol and dressed with mag. acid. salicyl. A pencil of CO₂ snow firmly pressed on a plantar wart for several minutes until a narrow zone of normal skin around the wart is frozen will be followed by a bullous reaction which permits the wart to be dissected away with ease in a day or two. The crater should be dressed as above. Large

plantar warts may be treated with x-rays, and success can be expected in about 80 per cent of cases. The treatment is painless, but an x-ray burn is not, and must be avoided by careful dosage. A previously untreated wart may be given a single dose of 600 to 800 r units through 1 mm. of aluminium at a kilovoltage of 90 to 120. Pain is usually relieved quickly, and the plantar wart should disappear in a month; if it does not, the dose may be repeated, but once only. A more cautious method is to give four doses of 200 r at weekly intervals exactly to the wart. Should irradiation fail it is important to avoid the use of strong caustics and cauterization, but the irradiated wart can safely be pared and kept under plaster. Ung. acid. salicyl. B.P. may be applied within a protective ring of felt.

DISEASES DUE TO ANIMAL PARASITES

Scabies.—The diagnosis of this common and troublesome disease may be easy and certain if typical burrows are present, or it may be so difficult as to 'baffle the most experienced dermatologist. Burrows should be sought in the creases of the wrist, of the ulnar side of the hand, and of the palm. It is not generally known how easily the acarus or ova can be demonstrated by wetting the burrow with 5 per cent solution of caustic soda or potash and then scraping out with a scalpel and examining the scraping under the low power of a microscope. Even if burrows are not found, an itching eruption of fine papules on the wrists, the inner sides of the arms, the axillary folds, the umbilical region, the pubic area, the inner sides of the thighs, and the ankles is almost certainly scabies, and a history of familial cases increases the probability. It should be remembered that a patient with factitious urticaria will produce urticarial lesions by scratching scabies, and in children papular urticaria is often vesicular or bullous; so is scabies, and both may show the same distribution. Lesions in the finger clefts are misleading, since cheiro-pompholyx, eczema, and intertrigo imitate scabies there.

Treatment of scabies.—When many treatments are advocated to cure a disease it usually means that none of them is satisfactory, but surely the exception to this aphorism is in the case of scabies. The present spate of new methods merely emphasizes the probability that any insecticide brought into intimate contact with every bit of infected skin will cure the infection. There are three essentials to success in the treatment of scabies. First, an attack upon the stratum corneum, which shields parasite from the insecticide and indeed provides a veritable Anderson shelter for the acari on the palms and soles. Thorough scrubbing with a nail-brush and lots of soap on several occasions is usually necessary, although the use of strongly alkaline or soapy solutions, which themselves soften and penetrate the horny layer, gives a fair measure of success without the scrubbing. But the easy way is not the best. Secondly, every part of the body must be treated with the insecticide, and it is obvious that the chance of missing small areas decreases with repeated applications. To prevent dermatitis venenata arising from treatment, a limit, determined by experience with each remedy, must be set to the number of these applications. The third essential is the disinfection of the underclothing and night apparel. Recent experiments have made doubtful the necessity for sterilizing the outer garments and bedding, but where facilities exist the extra precaution can do nothing but good. Contacts must be treated or reinfection is likely to occur.

The choice of an insecticide is dependent upon what is available, and due consideration should be given to economy. The derris root treatment described by Captain Saunders (*British Medical Journal*, 1941, 1, 624) is clean, simple, and economical; briefly, it consists of six applications in two days of the following lotion. One teaspoonful of soap flakes to 10 oz. of a mixture of 4 oz. of derris root powder in one gallon of cold water. The lotion of equal parts of benzyl benzoate, industrial methylated spirit, and soft soap has become very popular, and the official cream is less irritating and more acceptable to the patient. After soaping, scrubbing, and bathing the benzyl benzoate

lotion is painted on the wet skin and again when dry, and any residual lotion should be used up next day on the areas most involved and on the thick skin of the palms and soles. Sulphur is an excellent insecticide and is more potent in an alkaline medium. The effective but messy ointment need not be used. There are many new emulsifying bases which make non-greasy ointments and creams to which 10 per cent precipitated sulphur may be added. For example, 7 per cent of lanette wax added to a simple ointment enables the product to be creamed with water. Good results have been obtained with lotio calcii sulphurati diluted 1 in 10; with 10 per cent sodium thiosulphate followed by the application of dilute hydrochloric acid; and also with precipitated sulphur rubbed into soap lather and then into the skin. When sulphur is not tolerated 10 per cent balsam of Peru in zinc ointment will be found useful.

The reaction of the skin to these remedies is mainly follicular, and the appearance of a rash of irritating red dots marking the irritated follicles is often regarded by the patient as an extension of the scabies, so that treatment is continued and extensive dermatitis results. This should be treated with calamine lotion, to which 2 per cent of tar solution may be added. Luminal, gr. 1/2 b.d., helps to allay the irritation of the dermatitis or the psychic itch which lingers with imaginative folk long after the infection is cured.

PEDICULOSIS

Pediculi are often the cause of irritation of the scalp, body, and pubic area, and it is surprising how often their presence is overlooked.

Nits or pediculi in the scalp are a simple explanation of local irritation and of scratch marks across the shoulders. A lotion of phenol 3 per cent in liq. hydrarg. perchlor. should be applied liberally to the scalp, where it will kill the lice and prevent or cure septic infection. The same lotion will allay the irritation of the scratched skin.

Pediculi corporis should be looked for when a patient has soiled underwear, especially if by habit or necessity the clothing is worn night and day. Infested patients complain of irritation of the body, and excoriations and pigmented macules are often seen. The lice are to be found concealed in the seams of the underclothing, although in severe infestation they are present on the skin too. Various insecticide powders for dusting on the clothing provide a second-best method for the control of body lice, but the obvious solution is the improvement of personal hygiene and efficient disinfection of clothing and bedding.

The crab louse, *Phthirus pubis*, gives rise to an intense pruritus of the pubic area. The infection is often a venereal one, but it may readily be acquired from infected lavatory seats. Inspection of the pubic hairs, preferably with the aid of a magnifying glass, reveals the presence of the small dark nits close to the skin. It is not so well known that *Phthirus pubis* also attacks the axillæ and eyelid margins. Treatment is simple, and the phenol lotion mentioned for the treatment of pediculosis capitis will do for the pubic and axillary areas. The weak sulphur and mercurial ointments are also effective, but strong applications must be avoided. For example, ung. hydrarg. has been responsible for much dermatitis and discomfort. So has the unnecessary habit of shaving the pubic area. The liberal use of soap lather is very helpful, and no doubt a paste of it with precipitated sulphur would be an excellent remedy. The ova are less readily destroyed, but if treatments are repeated at intervals of a few days the infection is soon ended. Disinfection of the underclothing is necessary.

A plan for the abolition of coal smoke from our towns and cities within ten years from the end of the war is outlined in the autumn number of *Smokeless Air*, the journal of the National Smoke Abatement Society (temporary address: 94, Manor Green Road, Epsom, Surrey). The proposed scheme (published for discussion and not yet officially adopted by the society) is based on proposals already made for the creation of

smokeless central and other special zones as a part of post-war town planning, and suggests that in each town there should be a planned stage-by-stage extension of these zones until the whole town is smokeless. The rate of progress, especially when residential areas are reached, would depend primarily upon the rate at which increased supplies of smokeless fuels and appliances become available.

Treatment of Varicose Veins in Soldiers

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THE treatment of varicose veins by injections alone presents many difficulties when it is applied to military patients. In the first place, it is common for the affected veins to show the condition of *ectasia* rather than true varicosity, and veins of this type do not respond at all well to injection methods. Secondly, regular or systematic treatment is often quite impossible, owing to the continual movement of troops, re-postings, etc. A large proportion of soldiers reporting sick with varicose veins have had a few haphazard injections at irregular intervals; these may have had no effect whatsoever, or the benefit conferred was only temporary—a fact that has not escaped the soldier's notice and encourages him to distrust or to refuse further injection treatment.

Any form of operative treatment recommended must be considered in the light of its effect on the man's efficiency as a soldier, and precedence must be given to the method which is most likely to make him fit for full duty within the shortest possible time. Extensive radical excisions (Payne, 1941) have no place in the treatment of military patients. Apart from the long period of convalescence required, the scars which remain often form a basis for continued complaints.

The Trendelenburg operation, when it is not combined with injection, is frequently most disappointing. There may be little or no diminution in the size of the varices, or, alternatively, any improvement noted may be only temporary, as the affected veins dilate again, owing to the opening up of collateral anastomoses with the deeper channels. When combined with injection, the Trendelenburg operation has many advocates, and a 90 per cent cure has been claimed (Oldham, 1941) for this method of treatment. Many workers, however, including the writer, have not been so successful in the results obtained, in that the thrombosis is apt to be incomplete and patchy in distribution. Furthermore, a formal Trendelenburg operation is not to be undertaken lightly, and there is no question that military patients must be admitted to hospital.

SUBCUTANEOUS LIGATURE COMBINED WITH INJECTION

The accompanying photographs illustrate this method. In the case treated the varicosity involved the whole of the great saphenous system and had been present for 12 years. Complete thrombosis of all the dilated veins was obtained from one treatment.

In the method of subcutaneous ligature, a stitch is passed round the vein, and is tied over a swab placed on the skin surface. Except in cases where the varicosity extends right up to the saphenous opening (see below), the vein is ligatured at its *highest visible or palpable point*. This may be situated in the thigh (often at the junction of the upper and middle thirds) or at the medial side of the knee. In the former case a second ligature is applied at knee level. Very occasionally a third ligature is required.

An injection of sclerosing solution is made into the vein immediately below each ligature. The injected fluid takes effect in a 'closed' and relatively small segment of vein, where the blood is almost completely stagnant and there is no dilution from backflow. As the result an effective thrombosis is invariably obtained.

Technique of ligature.—The ligatures are most easily applied with the patient standing up. Silkworm-gut, threaded on a fairly fine curved skin needle, is employed. The needle is passed round the vein, transfixing the skin about 1/4 in. on each side of it, and the gut is tied over a small roll of gauze the thickness of a finger. A local anæsthetic is quite unnecessary.

Injection.—On the suggestion of Lieut.-Colonel S. Sokolowski of the Polish Army Medical Corps, 20 per cent saline solution has been used. This has the great advantage of being readily obtainable, and it has been most effective. Up to 50 c.cm. can safely be injected at one treatment, so that a widespread thrombosis can usually be obtained. Ten to 20 c.cm. is injected below each ligature, the amount depending upon the extent and varicosity of the veins under treatment. Cramping pain is felt in the limb about 15 seconds after injection; it may be fairly severe for 30 seconds, but usually passes off completely within 2 minutes.



Fig. 1.—Showing the extent of the varicosity.

If the dilatation extends right up to the saphenous opening, subcutaneous ligature is impracticable; an open ligature is therefore carried out, but no widespread dissection is attempted. The vein is exposed by a 1/2-in. incision at its highest point, and is divided. Ten to 20 c.cm. of saline solution is injected into the cut lower end before this is ligatured.

After-treatment.—The presence of the ligatures *in situ* causes comparatively little discomfort, and, considering the extent of the thrombosis produced, the reaction is not severe. It is customary, therefore, to return the patient to his unit, with a recommendation that he be excused all duties for 48 hours, and that he be kept on light duty until he reports back for removal of the ligatures in 7 days' time. Patients whose veins are very dilated are detained in hospital for one or two nights. During this time the limbs are firmly bandaged to compress the veins and to reduce the size of the ultimate thrombosis. Open ligature of the vein at the saphenous opening does not necessitate hospitalization provided that, in contrast to a formal Trendelenburg operation, it is done through a small incision and no

extensive dissection is attempted. After removal of the ligatures a further period of light duty may be required, depending upon the reaction present, but most patients can return to full duty within two weeks of the original treatment.

Results of treatment.—The immediate results are excellent. Of 150 soldiers treated by this method the great majority required only one treatment for each affected limb. About half the patients had two ligatures applied—one in the thigh and one at knee level. The rest, in whom the varicosity or ectasia did not extend above the knee, were treated by a single ligature at this level. As already stated, most of the patients returned to full duty within 2 weeks of the original treatment. The late results cannot at present be assessed, owing to the difficulties of follow-up in Service patients. It has not been possible to re-examine more than 30 patients, and these at intervals of from only 2 to 9 months after treatment. In these, however, the



Fig. 2.—Subcutaneous ligatures at A and B. The first injection was given as shown, and the second at the point marked C. Twenty c.cm. of 20 per cent saline was injected in each situation.

affected veins had all contracted down to hard slender cords, in which any possibility of re-canalization seemed to be quite out of the question.

DISCUSSION

It is maintained that the method of subcutaneous ligature combined with injection is particularly suitable to the treatment of military patients, in whom injections alone are unsatisfactory and all forms of radical operation are contraindicated.

The method is not, of course, a new one (Russell, 1941; McCurrieh, 1941), and I am aware that it has been extensively criticized (Eckhoff, 1941; McAusland, 1941; Schick, 1941; Oldham, 1941), mainly on the grounds that the saphenous vein cannot be ligatured at its highest point. Treatment by ligation at any lower level is stated (Schick, 1941) to be followed eventually by as high a percentage of recurrences as

after simple injections alone, and it has suffered the sweeping condemnation (Oldham, 1941) that it is as futile as would be the removal of the distal half of a hernial sac. The first assertion is at least open to question; the second can be categorically denied. Complete thrombosis of all dilated veins in the great saphenous system can usually be obtained at one treatment by two well-placed ligatures with an injection below each. Most patients return to full duty within two weeks of treatment, and hospitalization is rarely necessary. No claims are made regarding the late results. Fresh varices may undoubtedly develop in the years to come, as they may with any form of treatment. It is suggested that this, like other post-war problems, does not require serious consideration at the present time.

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The Treatment of Scabies

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A GREAT deal of confusion exists concerning the best methods of treating scabies. Every method has its advocates or detractors. Much of this confusion is caused by inaccuracies in diagnosis of infection and inaccuracies in assessment of cures. At the present time the disease is in the public eye, and many irritating skin conditions unconnected with *Sarcoptes* are apt to be diagnosed and treated as scabies, though, on the other hand, mild cases are often overlooked. Scabies can only be diagnosed with certainty when the mite *Sarcoptes scabiei* can be demonstrated or, at least, an unmistakable burrow seen. Another difficulty arises in assessment of cure. Many treated cases still show signs of extensive secondary impetigo or eczema even though the primary scabies has been cured. In such cases mild applications may cure the secondary complications and thus get the credit of curing scabies, which they are quite incapable of doing.

It is commonly believed that a long soak in a hot bath, followed by vigorous scrubbing, is an essential part of any scabies treatment and that this soaking and scrubbing will in itself often cure the disease. Results given below show that almost 100 per cent of cases of scabies can be cured if efficient medicaments are used without any bath or scrubbing at all. If a well-established burrow is soaked and scrubbed, the brush can be applied vigorously to the lesion for as long as ten minutes without dislodging the parasite, and unless the scrubbing is severe enough to draw blood it is unlikely that many of the mites will be removed in this way. Really thorough scrubbing, often repeated, may sometimes cure scabies (Dixon, 1941), but this does not appear to be a practicable method for general use. Gordon and Seaton (1942a), from their work on *Notoedres*, suggest that scrubbing may be an important preliminary part of scabies treatment. Their view is in part based on an examination of the lesions produced by *Notoedres*; these are covered with scabs and dry exudate, whereas in human scabies live mites are seldom so protected. In spite of this, however, it is desirable that before applying a parasiticide

the body should be soaked in a hot bath and rubbed well with soap, as this may enable the medicament to penetrate the skin more readily.

It is dangerous to assume that a patient has, or has not, been cured mainly because of the disappearance or otherwise of symptoms such as irritation. Some patients continue to itch for weeks after all parasites have been killed, while in other cases methods which we know to have practically no effect on the parasites will give at least temporary relief from irritation, especially if the patient believes they are efficacious. Many writers state that the methods they advocate will cure 'resistant' cases which have not responded to other treatments. We have found no indication that the parasites are much more difficult to kill in some individuals than in others. There are, however, as stated above, considerable differences in the rapidity with which symptoms such as itching disappear; but a more potent acaricide does nothing to allay these symptoms—it may easily have the opposite effect.

In our experiments on the treatment of scabies we have assessed our cure primarily by an examination of the adult female mites removed from treated cases. We have developed methods by which we believe that over 90 per cent of the ovigerous females can be detected. Samples totalling 1,200 mites removed from 441 cases suggest that about 90 per cent of the ovigerous females seen on examining the skin are alive, the remaining 10 per cent having died *in situ*. If only dead mites are found after treatment this suggests that the method is likely to be successful, but such results must be confirmed by a study of the relapse rate. Of 1,500 cases treated by us, approximately 1.7 per cent had a recurrence of scabies; but as only three individuals relapsed within ten weeks we are probably safe in assuming that the recurrences were mainly reinfections. (Incidentally, a further 2.6 per cent of patients returned apparently uncured a few days after treatment, but these were found to have no living *Sarcoptes* and merely a persistent itching, which gradually disappeared without further scabies treatment.) If, on the other hand, it is possible to find any live mites 24 hours after completing a treatment, this leaves no shadow of doubt that the treatment has not been successful. It should be noted that if even one live mite is left a recurrence of the disease is likely. It may take several weeks before the recurrence manifests itself fully, for this time must elapse before a reasonably large mite population can be built up again. Our results are based mainly on examination of the ovigerous females, but preliminary experiments suggest that the medicaments which kill these are also reasonably effective against the eggs. Incidentally, eggs killed with benzyl benzoate or sulphur seem to be 'fixed' and remain normal in appearance when incubated; we therefore find it difficult to interpret Gordon and Seaton's (1942b) results, for they assessed the potency of drugs against *Notoedres* by the percentage of eggs which degenerated after treatment. Nymphs, larvae, and adult males occur more superficially than females, and it seems unlikely that they will escape more easily. Timoney (1924) finds, with the *Sarcoptes* attacking the buffalo, that eggs are only slightly more resistant than adult females; all other stages are less resistant. We have also found that there is a very high mortality during development; if a proportion of live eggs are left deliberately they seldom give a reinfection. The chances of a reinfection where, say, 5 per cent of the eggs survive are exceedingly remote in all but those cases with abnormally high populations of *Sarcoptes*.

Several times the advocates of a new method have suggested that it is much simpler than the old one because fewer applications of medicament are needed or because the bath and scrubbing can be omitted. These statements have been made without testing the old method to see whether it might also work under the simpler conditions. The main errors in assessment of scabies treatment have thus often led to an under-estimation of the efficacy of old methods, while at the same time the efficacy of certain new methods has been greatly over-estimated.



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Details are given below of tests with most of the treatments in common use. In many cases the methods have been tried with and without baths and with and

without any scrubbing of the usual sites of election. In all cases the whole body, from the neck down, has been treated with the medicament. The results are

TABLE

A comparison of different methods used in the treatment of scabies. All results obtained 24 hours after the first application unless otherwise stated

Method	Bath	Scrub	Cases	Cure %	Mites dead	Mites alive	% mites killed
<i>A. Sulphur</i>							
(1) Sulphur ointment B.P. 10% ..	+	+	57	97	269	2	99.5
" " " 10% ..	+	—	64	90	331	9	97
" " " 10% ..	—	—	26	88	335	8	98
(2) Marcussen's ointment (kathiolan)	+	—	7	100	169	0	100
(3) Flowers of sulphur :							
Day 1	+	—	2	0	4	22	15
" 2	+	—	2	0	26	12	33
" 3	+	—	2	0	29	14	67
(4) Thiosulphate; HCl :							
Day 1	+	—	6	0	11	33	25
" 2	+	—	3	0	31	31	50
" 3	+	—	3	66	13	5	72
(5) Sulfomil :							
Day 1	+	+	5	0	20	96	17
" 2	+	+	5	0	22	63	26
" 3	+	+	4	0	42	46	48
(6) Internal sulphur : (10 days)	—	—	4	0	0	50	0
<i>B. Rotenone</i>							
(1) Derris root lotion :							
Day 1	+	—	13	15	121	44	73
" 3	+	—	13	46	81	22	79
(2) Rotenone emulsion 2% (sarevan)	+	—	4	25	559	171	76
<i>C. Benzyl benzoate</i>							
(1) 5% in spirit	+	—	5	40	225	23	91
(2) 10% " "	—	—	38	95	307	2	99
(3) 10% " "	+	—	64	94	737	6	99
(4) 20% " "	—	—	43	97.5	291	2	99.3
(5) 20% " "	+	—	52	98	301	1	99.6
(6) 25% " "	+	—	37	97	175	2	99
(7) Lotion (25% benz. benzoate, 35% soft soap, 40% spirit) ..	+	+	32	100	210	0	100
(8) " " " " " " " " ..	+	—	9	100	30	0	100
(9) 10% " emulsion"	+	—	12	43	128	16	89
(10) 10% " " " " " " " " ..	—	—	12	75	63	5	93
(11) 20% " (L.W.)	—	—	41	97.5	281	1	99.6
(12) 20% " " " " " " " " ..	+	—	50	98	368	1	99.7
(13) 20% " (S.T.)	—	—	41	100	474	0	100
(14) 20% " " " " " " " " ..	+	—	24	100	190	0	100
(15) 20% " (W.F.Z.)	—	—	48	100	415	0	100
(16) 20% " " " " " " " " ..	+	—	21	100	106	0	100
(17) All 20% " emulsions " ..	+	—	225	99	1,834	2	99.9
<i>D. Dimethyl-diphenylene disulphide</i>							
(1) Undiluted	—	—	6	100	178	0	100
(2) 10% in paraffin	—	—	3	100	81	0	100
(3) 5% " "	—	—	5	80	79	1	98.5
(4) 2% " "	—	—	2	50	62	47	57
(5) 0.5% " "	—	—	1	0	44	21	67
<i>E. Pyrethrum</i>							
(1) A.200 (extract in paraffin) ..	+	—	3	33	32	2	94
(2) Emulsion in water (2% total pyrethrins).	+	—	4	75	41	6	87
(3) Solution in paraffin (1% pyreth- rin I, approx. 1.75% total pyrethrins)—							
(a) Sprayed	+	—	9	22	91	28	71
(b) Painted	+	—	3	0	93	65	59

summarized in the table. The numbers of mites found may require some explanation. We hope to publish elsewhere particulars of the numbers of parasites observed in cases of scabies, but may state here that on an average there were only 12 adult females. The majority of cases have less than this number, and a very small minority have over 50. The percentage of mites killed by any method is approximately the same whether only a few parasites are found on many patients or whether a large number of parasites are found on a single patient. During the later part of the experiments certain substances which we knew to be effective—e.g. sulphur ointment—were frequently used on cases irrespective of the parasite population, so that only rather small numbers of mites could be removed after treatment. With other methods of less-well-established efficacy, cases with high parasite count were chosen in order to obtain results quickly and to avoid a mass of work in treating or re-treating cases. All patients studied were adult males, but observations made on children and females do not suggest any considerable differences.

SULPHUR PREPARATIONS

Sulphur ointment (10 per cent sulphur).—Sulphur has been used since ancient times (Hebra, 1868) for the treatment of scabies, and sulphur ointment is a sarcopticide of proved efficacy. It has gained some notoriety because, when over-applied, a severe itching dermatitis is produced which is often thought to be due to a continuation of the parasitic infection. More ointment is then applied, with a further aggravation of the condition and, finally, disastrous results. The standard treatment consists in making three applications of the ointment, the first (and sometimes the second and third also) following a hot bath and scrubbing. Before our investigation reached the present stage, in which we can locate and extract most of the parasites, about 200 cases were treated by the above method without a single relapse being detected. In 147 cases since treated, the mites have been extracted after treatment. The results given in the table show that a very high proportion of the mites were killed by one application, using approximately 3 oz. of sulphur ointment per patient. There is some indication here that the efficacy of the treatment is slightly enhanced by bathing and scrubbing, although the difference between the results (percentage killed) from the two types of treatment is not statistically significant. Even without bathing and scrubbing, very few mites survive, and two applications of the ointment have cured 100 per cent of the cases. When skilled orderlies are available the disadvantage of the messiness of the treatment often outweighs the ease with which the medicament can be applied. We are of the opinion that sulphur ointment is likely to give more satisfactory results than other methods when used by the unskilled, for even if the ointment is carelessly applied there are chances of its spreading over a wider area than was originally covered. Adequate warning should be given against over-treatment. We have seen cases which have not been cured after using sulphur ointment for many days; these patients have been applying the ointment locally on the irritating areas. It cannot be too strongly stressed that the whole of the body except the head must be covered.

Sulphur vanishing cream.—In order to avoid the messiness of sulphur ointment and to economize in the paraffin base, vanishing creams containing sulphur, obtained through the kindness of the Cooper Technical Bureau, have been tried. The creams are very pleasant to use and do not soil the garments unduly. One containing 10 per cent of sulphur appears to be as effective as the ordinary ointment. Further research is in progress to try to decrease the sulphur content; in 12 cases treated with a 0.5 per cent sulphur vanishing cream the majority of the parasites were killed.

Marcussen's ointment.—A commercial preparation of Marcussen's ointment called 'kathiolan' was received through the kindness of Messrs. C. Zimmerman. It is claimed that this preparation will cure scabies within

24 hours, a contention which our experiments support. If applied as thickly as advised by the manufacturers, this ointment is even more objectionable in use than ordinary sulphur ointment, but if employed more sparingly it is equally effective and no more messy than the latter.

Flowers of sulphur.—Flowers of sulphur dusted over a patient are said to give a simple and effective cure. The table shows that though this treatment does kill some of the parasites it is relatively ineffective; for after 24 hours very few mites have been killed, and even after 3 days one-third of them are still alive. It should be noted that our patients have remained in bed in contact with the powder, 60 g. of which was used for each case. It seems likely that treatments of this kind result in a race between the production of a dermatitis and the extermination of the parasite. There is a real danger that the dermatitis may develop first.

Sodium thiosulphate and hydrochloric acid.—It has been thought that if the sulphur could be released in nascent form it might be particularly effective. In this method the patient is first painted with a strong solution of hypo, which is allowed to dry. Some acid (i.e. hydrochloric) is then applied to the body; sulphur is released and conditions very harmful to *Sarcoptes* are alleged to arise. It should be noted that a patient who has been treated in this way is covered with yellow powder. This shows that the sulphur is deposited in rather coarse granules and not in a finely divided state, for in the latter condition the deposit would be white and not yellow. We find that one application of these solutions is hardly more effective than dusting with flowers of sulphur, and even after three applications a substantial proportion of the parasites remain alive. This method is troublesome to use, and the results are so unsatisfactory that we can see no reason for continuing with it. Moreover, it lends itself to zealous over-treatment.

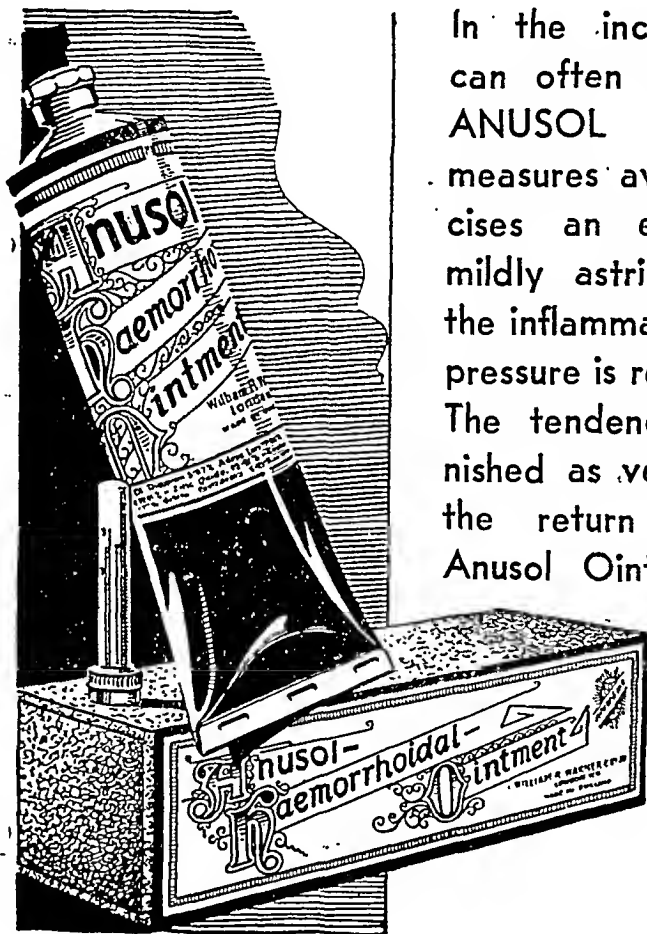
Sulphur lather tablets.—Sulphur lather preparations have been used with apparent success in America (Nolan, 1938), and samples of a similar preparation ('sulfomil') were received through the kindness of Messrs. Glaxo Laboratories Ltd. In preliminary tests these appeared to give favourable results, for patients stated that the itching was greatly relieved and no sign of any dermatitis was produced. When, however, the effect of this preparation on the parasites was assessed with greater accuracy it was not found to be more effective in killing the *Sarcoptes* than the other medicaments which deposited sulphur powder on the skin. Even after three daily applications a substantial proportion (about 50 per cent) of the parasites were still alive.

Sulphur taken internally.—One of us has already reported (Mellanby, 1941) that sulphur taken internally appears to have no effect on *Sarcoptes* in the skin. Even if sulphur is taken in as large a dose as can be consumed without causing severe physical discomfort (10 g. daily for 10 days) the parasites appear to be entirely unharmed at the end of the period, and fresh mites can be induced to burrow normally.

DERRIS ROOT PREPARATIONS

Derris root lotion.—Rotenone, which is one of the active insecticidal products from derris root and some other plants, is known to be very effective in killing many species of insects. We are informed by the Cooper Technical Bureau that tests of rotenone-containing preparations against scabies in animals have given unsatisfactory results, although these products are highly effective against insect parasites on the same animal. Further, derris is notorious for causing dermatitis in man, and unless it has substantial advantages in the treatment of scabies its use is not one which recommends itself. The derris root lotion is essentially a suspension of derris root in water (4 oz. of derris root, 1 gallon water, a small quantity of soap flakes). The results show that it is fairly toxic to *Sarcoptes*, but even after three days 21 per cent of the mites survived and about 50 per cent of the patients still

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harboured *Sarcoptes*. This result is much inferior to that obtained by one application of sulphur ointment. Incidentally, we obtained derris root of known rotenone content through the Cooper Technical Bureau; samples bought in the ordinary way show considerable variations in strength.

Rotenone emulsion.—A 2 per cent emulsion of rotenone called 'sarevan' advocated for the treatment of scabies was obtained through the kindness of Messrs. Evans Sons Lescher and Webb, Ltd. It is interesting to compare the proportion of rotenone in this product with that found in other medicaments. The usual strength used in animal dips in veterinary practice is 1 in 16,000; the derris root lotion mentioned above contains approximately 1 part in 1,000; sarevan contains 1 part in 501. Notwithstanding this relatively enormous concentration we have not found sarevan outstandingly successful. A number of patients were treated with 4 applications, as recommended by the manufacturers, and a satisfactory cure was obtained, but some of them developed an intractable scrotal dermatitis. One application of sarevan still left about a quarter of the mites alive, so this method also was found to be much less effective than sulphur ointment.

BENZYL BENZOATE

Benzyl benzoate is by no means a new treatment for scabies. It is the main active ingredient in balsam of Peru, which has been used for a very long time. Benzyl benzoate itself, in the form of 'percol', was advocated by Sachs and Juliusberg as long ago as 1900. This medicament was, however, first popularized by Kissmeyer, who in 1937 reported very favourable results from its use. Our conclusions support Kissmeyer's results, but we find that in unskilled hands, with insufficient supervision, benzyl benzoate lotion may be applied in such a way that some burrows are missed and relapses are apt to occur.

Benzyl benzoate lotion (25 per cent benzyl benzoate, 35 per cent soft soap, 40 per cent spirit), the usual form in which this compound is applied, was found to be 100 per cent effective, and equally satisfactory cures were obtained whether or not the patient was scrubbed. As there is some difficulty in obtaining soft soap and spirit, other benzyl benzoate preparations have been tried. A simple solution in methylated or industrial spirit was very effective, even as low a concentration as 10 per cent benzyl benzoate killing 99 per cent of the parasites. A solution containing only 5 per cent proved less satisfactory, though more efficient than any other anti-scabies treatment except sulphur ointment. A solution in spirit is more difficult to use than the benzyl benzoate lotion as it is not easy to distinguish which parts of the body have been covered.

Results of benzyl benzoate emulsions in water have also been tried. Several different emulsifying agents, including lanette wax S.X., cellofas, and stearic acid with triethanolamine, have been found equally effective. An emulsion containing 10 per cent of benzyl benzoate appears to be on the weak side, giving results closely resembling those obtained with a 5 per cent solution in spirit. It should be noted that the emulsion goes considerably further than the spirit solution, only 2 fl. oz. being required to cover the body, as against 3½ oz. of spirit solution. This means that approximately the same amount of benzyl benzoate is applied to the body with a 10 per cent emulsion as with a 5 per cent solution. A 20 per cent emulsion appears to be completely satisfactory.

The National War Formulary gives a benzyl benzoate emulsion containing 25 per cent of benzyl benzoate and 2 per cent lanette wax S.X. The formula in the Appendix to this paper seems to us as efficient, and if many cases have to be treated it will effect important economies.

OTHER SARCOPTICIDES

Dimethyl-diphenylene disulphide (*dimethylthianthrene*).—This substance, which was formerly marketed by Messrs. Bayer under the name of 'mitigal', was obtained through the kindness of Imperial Chemical Industries Ltd. It is normally used undiluted on the

body; it does not seem to produce any dermatitis or discomfort, and kills 100 per cent *Sarcoptes* after one application. Unfortunately the substance is expensive in normal times, and at present is practically unobtainable. Preliminary experiments suggest that even when diluted down to 5 per cent in medicinal paraffin it is still efficient. Work on dimethyl-diphenylene disulphide emulsions in water is now in progress.

Lethane.—Organic thiocyanates, such as lethane, are very effective against lice, and it has been suggested that they will also kill *Sarcoptes*. A 2 per cent solution of lethane in medicinal paraffin appears to kill only about two-thirds of the mites after one application. Stronger solutions (i.e. 10 per cent) cause the patient very considerable discomfort, and still are less efficient than benzyl benzoate or sulphur ointment.

Pyrethrum.—Various pyrethrin-containing substances have been tested. A commercial preparation containing pyrethrum extract in a petroleum jelly ('A.200') was obtained through the kindness of Messrs. Mitchell Cotts and Co. Later, substances of accurately determined pyrethrin content were prepared by Dr. J. T. Martin of the Department of Insecticides, Rothamsted Experimental Station, Harpenden. These tests do not suggest that pyrethrum extracts are particularly valuable against human scabies.

Betanaphthol.—Only two cases were treated with 10 per cent betanaphthol ointment. Twenty-four hours after treatment 27 mites were removed; of these, 5 (18.5 per cent) were alive. As only 2 live mites were removed from the 225 cases treated with 20 per cent benzyl benzoate emulsion, it is clear that betanaphthol is a much less satisfactory medicament.

DISCUSSION

The experiments described above indicate that of the treatments of scabies in common use two only, sulphur ointment and benzyl benzoate, are satisfactory. It is interesting to compare the *in vitro* reactions of *Sarcoptes* to these preparations. It is well known that the mite will survive for several days when stuck in sulphur ointment on a glass slide; we have confirmed this observation. Sulphur ointment appears to be effective only when some active products due to the interaction of the sulphur and the human body are liberated. Benzyl benzoate, on the other hand, is rapidly lethal to the mites, which are killed within five minutes of contact away from the body.

It should be noted that it is almost impossible for a patient to apply either liquid preparations or creams satisfactorily to himself; therefore, if it is not possible to get another person (preferably trained for the purpose) to apply these remedies, it is better to use sulphur ointment treatment.

APPENDIX: DIRECTIONS FOR PREPARATION OF BENZYL BENZOATE EMULSIONS

The following three emulsions containing 20 per cent of benzyl benzoate have been found satisfactory. If a 25 per cent emulsion is preferred this can be made by increasing the benzyl benzoate and decreasing the water in the appropriate quantities.

Benzyl benzoate ..	200 mls
Lanette wax S.X. ..	10 g.
Water ..	800 mls

Melt the lanette wax on a water-bath, add the benzyl benzoate, and heat the mixture to a temperature of between 60° and 70°C. Pour the mixture into the water, previously heated to the same temperature, and stir until cold.

Benzyl benzoate ..	200 mls
Stearic acid ..	20 g.
Triethanolamine ..	5 mls
Water to produce ..	1,000 mls

Melt the stearic acid with the benzyl benzoate on a water-bath. Mix the triethanolamine with half the quantity required of warm water, and pour into the stearic acid-benzyl benzoate mixture cooled to about

30°C. Shake to form an emulsion. Add enough water to produce the required volume.

Benzyl benzoate 200 mls
1 per cent solution of cellofas W.F.Z. 800 mls

Shake together to form an emulsion. Put through a cream-making machine or homogenizer.

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The Cure of Scabies, and a New Remedy

By G. H. PERCIVAL, M.D., Ph.D., F.R.C.P.Ed., D.P.H.
(From the *British Medical Journal*, Vol. II,
17th October, p. 451)

THE time required to destroy an acarus infestation may not be long enough to allow the structural disorganization of the epidermis caused by the parasite to have righted itself entirely by the end of the treatment period. A treated case of scabies may be free from acari—that is to say, cured of scabies—but need not present a skin entirely free from lesions. Immediately after successful treatment with any of the recognized remedies scratch marks and pin-head blood crusts, subsiding pustules, crusts, and scaly tags may still be seen on the abdomen, buttocks, thighs, and anterior axillary folds. Such residues are less pronounced after the use of ointment preparations than when the remedy has been employed in the form of a liquid to be painted on the skin. While the presence of lesions following treatment does not mean that the object has not been attained, the absence of itching may not indicate a cure, for this symptom may disappear temporarily in a case in which treatment has failed, only to return in about ten days, during which time the surviving parasites have increased sufficiently to cause symptoms. The discovery of live acari at the end of a period of treatment proves its failure at once, but failure to find the acarus immediately is no proof of cure. It can only be regarded as such if repeated examinations over a period of two weeks are negative. By this time, however, if cure is not complete, lesions and symptoms will have developed which will be visible to the naked eye and obvious to the patient, except in the very rare instances of latent scabies, if such a state exists.

OBSERVATION PERIOD AFTER TREATMENT

The majority of cases of scabies to which one or other of the known efficient remedies are adequately applied are cured, and in them no acari would be discovered. In a few uncured cases, and perhaps in a given series in all uncured cases, no acari might be found immediately after treatment, and a period of observation would be necessary to demonstrate their continued presence. Only in a very few cases can the discovery of acari immediately following treatment, and not the failure to demonstrate their presence, at once give the desired information as to the result. It follows, therefore, that only in an extremely small proportion of cases can the observation period be dispensed with if the result is to be established with certainty.

This observation period subsequent to treatment of scabies is necessary and of practical importance only

when the value of a new drug is first being assessed. If it is then established that a drug in a definite concentration is capable of curing the disease when tested on a reasonable number of cases and following a definite routine, the criterion of cure, for practical purposes, when the drug is used in conditions where known new cases are numbered monthly by the thousand in a single community, is the efficiency with which the prescribed routine of application is carried out. In a large treatment centre it is not possible either to examine for acari closely enough for the examination to be of any practical value or to multiply visits by insisting on the period of observation. Apart from staff shortage, it is difficult to obtain regular attendance during the treatment period.

It cannot be asserted that the prescribed technique of treatment with any remedy is capable of success in every case, but failures following the correct application of sulphur ointment are extremely rare (Mellanby *et al.*, 1942). When the patient personally carries out the instructions the percentage of failures depends on his intelligence, home surroundings, and the care with which the instructions have been explained to him. A patient may reasonably be expected to be able to take a teaspoonful of cough mixture three times daily, and failures in the technique of this procedure must be few indeed. Similar success in the carrying out of instructions is not met with in the treatment of scabies or, for that matter, in the treatment of skin disease in general.

CHOICE OF REMEDY

The technique of the commonly used remedies is more or less similar and the choice has up to the present been governed by cost, cleanliness, time, and freedom from irritant properties. It may be, however, that the availability of the remedy will become the deciding factor.

Sulphur is the oldest remedy for scabies, and according to Hebra its indirect use dates back to the cure of Naaman's presumed attack of the disease. Its outstanding worth as an agent lethal to the mites and eggs of the acarus has been demonstrated recently by Mellanby, Johnson and Bartley (1942). It should be noted, however, that the standard treatment for scabies is not three applications of sulphur ointment as stated by them. Authors differ slightly in the technique advised. That laid down by Walker and Percival (1939) is six applications of 5 per cent sulphur ointment over a period of three days, preceded and followed by a bath, no bath being taken during the period of application. Sulphur is cheap and can be incorporated in a more elegant base than lard or soft paraffin if so desired, but to be efficient it must be applied in the form of an ointment to be rubbed in. This necessary use of fats and oils in conjunction with sulphur at a time when these substances are in short supply justifies the trial of possible substitutes which do not require fats and oils in their application or which need a less amount.

TETRAETHYLTHIURAM MONOSULPHIDE

Another substance has recently suggested itself as possibly being of use. There is no reason to anticipate a shortage in its supply, and this fact alone should recommend its trial on a large scale. This substance is tetraethylthiuram monosulphide, and since 1940 I have used it in the treatment of human scabies. Because of unavoidable delays it has been employed in only a small number of cases. It was found to be non-irritant to the human skin when applied in the form of pure powder, and no case of cutaneous idiosyncrasy to it has been encountered. It has proved curative in a strength of 5 per cent in the form of a liquid preparation in 50 consecutive cases, 21 of which were treated as in-patients in the ward of the skin department of the Edinburgh Royal Infirmary, and 29 as out-patients at scabies treatment centres. Of 25 cases treated with a 0.25 per cent solution 4 were cured; 1 case was treated with 5 per cent tetraethylthiuram monosulphide in a vanishing cream and was

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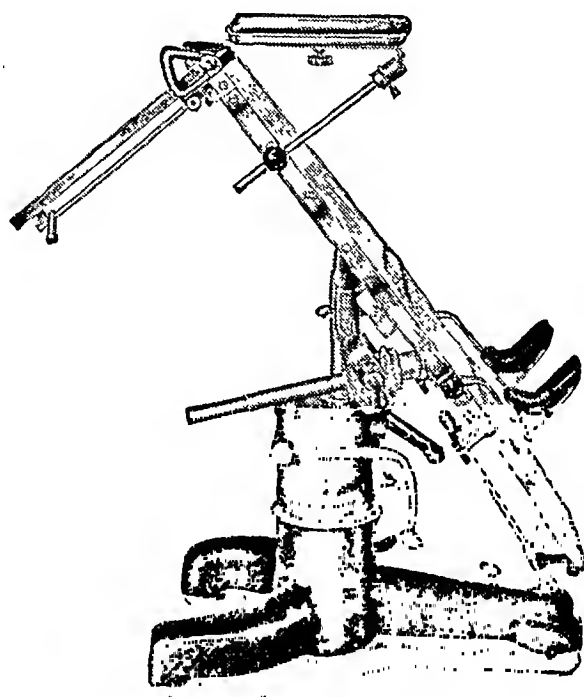
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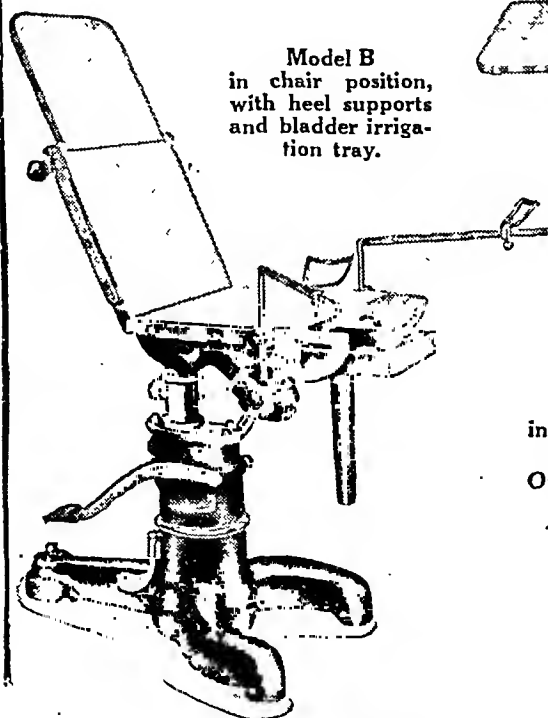
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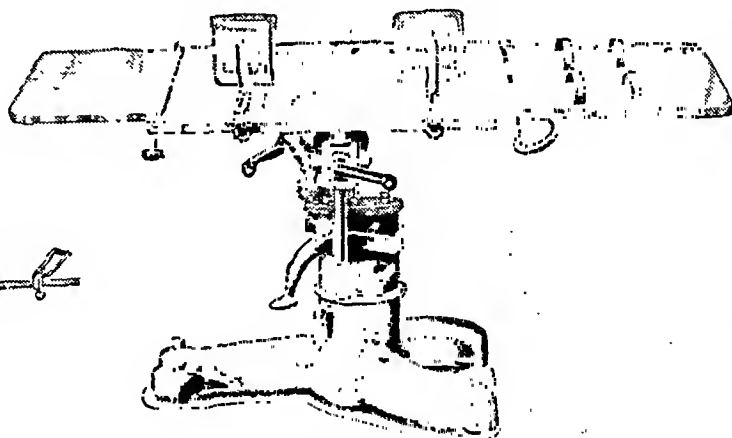


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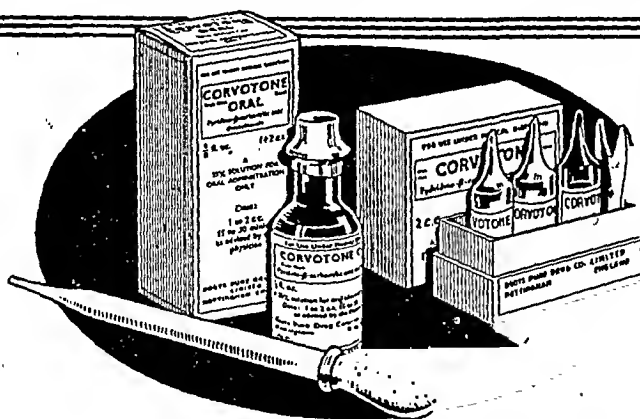
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cured; 3 were treated with a prepared tetraethylthiuram monosulphide powder mixed with water to form a paste, which was then smeared on the skin, and 1 was cured. The liquid preparation used was an emulsifiable oil having the composition: tetraethylthiuram monosulphide 25 per cent., polyglycerol ricinoleate 10 per cent., industrial methylated spirit 65 per cent. One part of this oil was added to four parts of water immediately before use. While the 25 per cent concentration remained stable at room temperature it tended to crystallize out if kept at lower temperature, but gentle heating sufficed to redissolve the crystals. Unfortunately the diluted oil separated, giving a layer of pasty consistency which did not redissolve. This necessitated preparing the required 5 per cent dilution immediately before use. The 25 per cent solution may stain material yellow, but this discoloration washes out easily. The mixture has a slight odour, not noticeable, however, in the 5 per cent dilution.

The liquid preparation was rubbed over the whole body, with the exception of the head, face, and neck, twice daily for three days, as in the case of sulphur ointment. The duration of treatment is an important point in the cure of scabies with any remedy, and repetition reduces the possibility of inadequate application. If staffed by a trained personnel, the scabies treatment centre can be relied on to ensure at least one adequate application even if there are difficulties in enforcing the necessary return visits (Percival, 1941).

Observations by Gordon and Seaton (1941) on the lethal properties of tetraethylthiuram monosulphide for acari in animal scabies have shown that it is more toxic for the mites and eggs and more rapid in its action than either benzyl benzoate or dimethylthianthrene (mitigal). During their experiments they were also able to prove conclusively that mites, especially larvae, can migrate from their burrows and infect surrounding clothing, which is capable of reproducing the disease if applied to another animal. These experiments on the possible transmission of animal scabies cast some doubt on the advisability of omitting to disinfect clothing in the case of human scabies, a view originally advocated by Mellanby (1941) although later modified by him.

SUMMARY

Tetraethylthiuram monosulphide in a concentration of 5 per cent is capable of curing human scabies. So far it has been found to be non-irritant to the human skin, and no instance of cutaneous idiosyncrasy to it has been encountered. It is cheap, clean, easily available, and economizes in fats and oils. Its trial on a more extensive scale by independent observers is suggested.

The author thanks Imperial Chemical Industries (Pharmaceuticals) Ltd., Manchester, for preparations of tetraethylthiuram monosulphide.

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Postural Instillation : A Method of Inducing Local Anaesthesia in the Nose

By A. J. MOFFETT

(Abstracted from the *Journal of Laryngology and Otology*, Vol. LVI, December 1941, p. 429)

THE usual methods of inducing local anaesthesia in the nose are often ineffective because of anatomical abnormalities, polypi or the presence of pus. The author describes a technique which is designed to produce a deep and lasting anaesthesia, and in which

bleeding is reduced to a minimum. It is safe and simple to administer.

Special instruments.—5 cm. angled serum needle with a closed blunt end, with three lateral holes near the end, to fit a 2 c.cm. syringe.

Anæsthetic solution.—3.0 per cent solution of cocaine hydrochloride in 0.5 per cent solution of sodium bicarbonate, freshly prepared. 3.5 c.cm. to 5 c.cm. of cocaine solution is sufficient, depending on the magnitude of the operation. 1 c.cm. 1/1000 adrenaline solution is added to 4 c.cm. cocaine solution.

Pre-medication.—Morphia 15 mg. one hour before operation.

TECHNIQUE

1. The patient lies on a couch on his left side with a pillow under the left shoulder, and the head depressed in a strictly lateral position to an angle of at least 45°. Take one-third of the prepared solution. Allow three drops to fall on each side of the nasal septum. Engage the needle half-way along the floor of the nose and instil half of the solution remaining in the syringe on each side. Leave the patient in position for 10 minutes. Occasional sniffs with the nostrils pinched allow the solution to enter the sinuses.

2. Instil half of the remaining solution as in (1). The patient then pinches his nostrils and rolls over on to his face and remains in that position for 10 minutes without relaxing his grip on his nose.

3. The patient rolls on to his right side. The nostrils are released. Position and instillation of remainder of solution as in (1). Position maintained for 10 minutes.

4. The patient lies on his back. Any unabsorbed fluid flows to the back of the nasal cavity and completes anaesthesia there.

Injection of procaine into the columella and the floor of the nose is needed for septum operations.

Pneumonia treated with Sulphapyridine and Sulphathiazole

By F. K. HERBERT

and

E. F. DAWSON-WALKER

(Abstracted from the *Lancet*, Vol. II, 8th August, 1942, p. 145)

THE work reported in the present paper was started early in 1940, at a time when little was known of the pharmacology of sulphathiazole. Of 30 cases of pneumonia, 16 were treated with sulphathiazole and 14 with sulphapyridine. There was no epidemic of pneumonia during the period of study and types of pneumococci varied widely. The series was too small for an assessment of the relative therapeutic value of the two drugs, but full data are given for the concentrations of the free drugs in the blood throughout the treatment. Doses were given four-hourly. The usual dosage for sulphapyridine was 2 g. for the first three doses, then 1 g. continued every 4 hours until the temperature had definitely settled and the clinical condition was improving. This dosage was also used for the first six cases treated with sulphathiazole; the other ten sulphathiazole cases received double the amount.

Both drugs produced defervescence and clinical improvement, the temperature falling to normal after 8-56 hours (usually within 24 hours). There was no significant difference in the rate of defervescence between the groups treated with the two drugs and no apparent relation between the rate of defervescence and the concentration of the drug in the blood. Vomiting and urinary abnormalities occurred with both drugs.

With both sulphapyridine and sulphathiazole the concentration of the drugs in the blood on a given dosage varied very widely in individual cases, but there were definite differences between the typical results with the two drugs. With sulphapyridine there was

usually a steep rise of the drug in the blood during the first 20 hours and later either a further gradual accumulation, or a steady plateau, or occasionally a falling curve. The peak levels varied from 4.6 to 20.7 mg. per 100 c.cm. With sulphathiazole in the same dosage the usual result was a rise during the first 14 to 34 hours to a peak of from 5 to 9 mg. per 100 c.cm. and a falling curve later. With the exception of one curve in the case of an old man who died, there was not the steady accumulation of the drug which is usual with sulphapyridine. In the 10 cases

treated with the double dosage of sulphathiazole there was steep initial rise to a peak during the first 10 to 20 hours, followed by a rapid fall, and in some instances a secondary rise later. These differences between sulphathiazole and sulphapyridine in the blood are attributed to the more rapid excretion of sulphathiazole.

The authors review other published studies covering large numbers of cases, and they conclude that sulphathiazole has no advantage over sulphapyridine in effectiveness, though it has less tendency to cause vomiting.

Reviews

DISEASES OF THE HEART. DESCRIBED FOR PRACTITIONERS AND STUDENTS.—By Sir Thomas Lewis, C.B.E., F.R.S., M.D., D.Sc., LL.D., F.R.C.P. Third Edition. 1942. Macmillan and Company, Limited, London. Pp. xx plus 297. Illustrated. Price, 15s.

This volume has come to be regarded as the standard work upon cardiology in the English language.

Sir Thomas Lewis has done for cardiology what free minds in medicine have long wished could be done authoritatively in other branches.

He has tried all things in heart diseases and held first to that which was good, not suffering himself to copy statements from older books, which he has not found to be true in practice.

The great value of a monograph or work upon a single subject by an exponent of it lies first in the author being able to discard the views, shown to be false by experience but sanctified by age-long acceptance, which clutter textbooks and which their authors seem fearful to omit; secondly, it lies in the expert's capacity of measured appraisal of recent work which the same conservatism will prevent reaching the textbook for a decade.

Perhaps the most valuable sentence in this book is as follows: 'it is reasonable to conclude that the burdens imposed by physiological acts upon the normal heart, however heavy these burdens may be, never injure the heart's fibres, never produce injurious dilatation, and never exhaust the heart's reserve'.

It may be hoped that this sentence and the careful reasoning upon which it is based will do much to dispel a belief which has been an unconscionable time adying among doctors, and is of course invariably held by laymen.

If the happy diminution of interest in the detail of cardiac murmurs which followed the last war is followed, after this war, by an appreciation of the truth of Lewis's teaching, the 'medicogenic' cardiac neurotic will become a rarity.

C. M. S.

CARDIAC SYMPTOMS IN THE NEUROSES.—By Doris M. Baker, M.D., M.R.C.P. (Lond.). 1942. H. K. Lewis and Company, Limited, London. Pp. vi plus 49. Illustrated. Price, 4s. 6d.

In this monograph the author sets out the conclusions of an investigation into the significance of such symptoms as left mammary pain, sighing respiration and palpitation, 'le trepidé' of Gallavardin. Dr. Baker has endeavoured to determine their significance and importance, whether any one of the three could be associated with organic disease, and to evolve a syndrome which would allow cases with no organic basis to be recognized.

Unfortunately she ignores the existence of a syndrome differing from what she describes only in that it is diagnosed in wartime, in males in khaki—soldier's heart or effort or Da Costa's syndrome ably described by Paul Wood in his Gaultonian lectures of 1941.

We feel that more might have been made of the investigation. Is the præcordial tenderness not due to the impact of the apex upon intercostal muscles in a

fibrositic subject and had the patients not evidence of fibrositis elsewhere? Is not the complex of palpitation, flatulence, giddiness and inability to draw a deep breath due to the neurotic habit aerophagy? Such may well be the proximate causes of these symptoms but is not the remote cause in the psyche.

The statistics might have been set out more clearly and convincingly, and in the table on p. 18 the symbols P and y² are not explained.

The argument is not really advanced by the illustration of a normal electrocardiogram.

Such phrases as 'overtired, upset or in a lowered condition of health' and 'mental strain and overwork' are out of place in a scientific appraisal of symptoms.

They smack of that confusion of thought, invariable in the lay mind and not uncommon in medical minds, which springs from the fact that our language—the language of Shakespeare—cannot find two words for two entirely distinct things, (a) those anatomical structures, the nerves and (b) the emotions which produce psychogenic symptoms.

C. M. S.

A SHORT PRACTICE OF OPHTHALMOLOGY (ANCIENT AND MODERN).—By Dr. K. Krishnamurthy and Dr. N. K. Bidyadhar. 1941. The Ophthalmological Books Publishing Company, Chodavaram, Vizagapatam District, India. Pp. viii plus 278. Illustrated. Price, Rs. 6

The authors point out that this book differs from the rest of its kind in that it aims at helping practitioners and medical students to compare modern and ancient ophthalmology. The sections on ancient ophthalmology embody the result of investigations by Dr. Bidyadhar and represent largely the teachings of the world's first ophthalmic surgeon Susruta of India's antiquity. They are of great interest rather than of practical use in the ophthalmology of to-day. The sections on modern ophthalmology deal with the anatomy and physiology and the various diseases of the eye. In addition there are special articles by prominent ophthalmic surgeons practising in India. These are reprints from recent ophthalmic literature both Indian and foreign, and these include articles on cataract, the evolution of cataract surgery, the intra-capsular extraction in senile cataract by tumbling of the lens, pitfalls for beginners of the cataract operation, some observations on primary glaucoma, keratomalacia, ocular complications in diabetes mellitus, tuberculous affection of the eye, ocular manifestations and complications in infectious diseases and their treatment, vitamin B, C, D in ophthalmology, chemotherapy in ophthalmology, physical therapy, ultra-violet ray therapy in eye diseases, short-wave therapy in eye conditions, protein shock therapy, ionic medication in ophthalmology, radium and roentgen ray therapy in eye diseases, some observations on hysterical eye conditions, modern methods of anaesthesia and analgesia in ophthalmic operations, the surgical treatment of detachment of the retina, corneal grafting, tarsectomy in trachoma, the surgical treatment of high myopia, Webster's operation for entropion, and the importance of systematic examination in ophthalmic practice.

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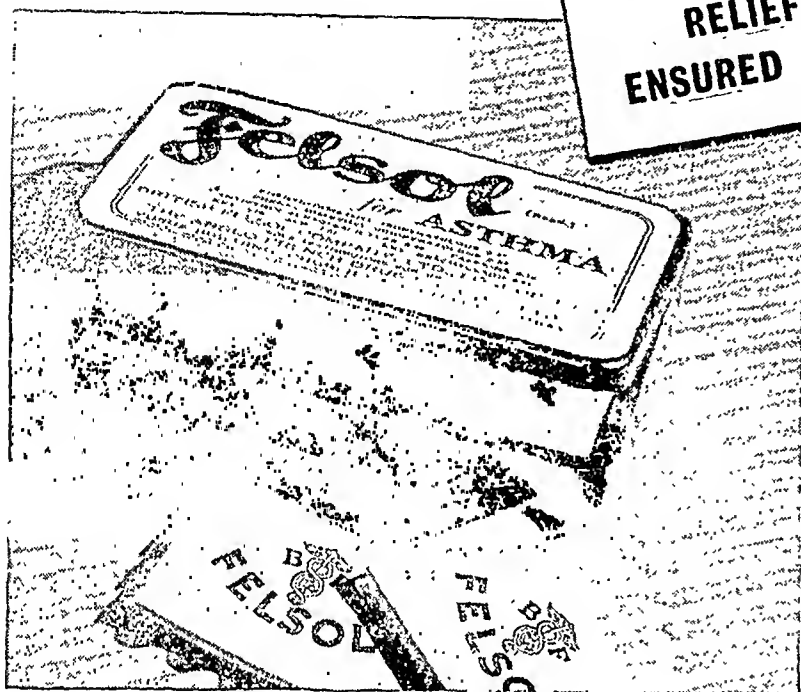
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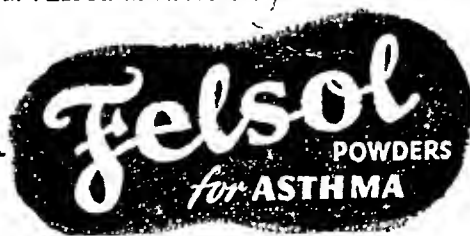


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The authors do not intend the book to be of the nature of a textbook, but rather to be a compendium of useful and practical information for junior ophthalmic surgeons and general practitioners, and in this they have succeeded.

To the ophthalmic surgeon the book will be found most interesting especially Susruta's technique for the couching of cataract. Considering the cheap price of the book, it is well brought out, and the paper and printing good. We recommend it as a useful book to medical men interested in eye work in India.

E. O'G. K.

A HANDBOOK OF OCULAR THERAPEUTICS.—By Sanford R. Gifford, M.A., M.D., F.A.C.S. Third Edition. 1942. Henry Kimpton, London. Pp. 410. Illustrated with 69 engravings. Price, 20s.

It is four years since the second edition of this book appeared, and during this period there have been many advances in ocular therapeutics. The original intention of the author was to produce a concise book on therapeutics, including the essentially valuable procedures in treatment and ignoring the purely traditional ones. Discussion of the pathogenesis and diagnosis of disease has, as far as possible, been avoided, and the surgery of the eye is discussed only as far as the indications for operation are concerned except for certain minor procedures which are needed in ordinary routine work.

In the third edition there is a complete re-writing of the section on vitamins. The effects of vitamin B₁ in toxic amblyopia and the corneal changes due to riboflavin (vitamin-B₂) deficiency are discussed. The rationale, importance and special indications for the use of sulphanilamide, sulphapyridine and sulphathiazole are considered. The author wisely points out that failure to give effective doses in early cases was due to fear of the toxic effects of this group of drugs. His opinion on the use of sulphanilamide in trachoma can be summed up by saying that it is useful especially when acute inflammatory symptoms and corneal ulceration are present, and that vision may improve considerably when these conditions clear up, but that the conjunctival lesions which often show improvement during treatment remain in most cases unchanged, and can certainly be made to improve much more rapidly by the use of local applications such as copper sulphate. It would seem, therefore, that at present the best treatment for trachoma is a combination of the use of sulphanilamide and local measures.

Reference is made to the sympatho-mimetic and parasympatho-mimetic drugs, to the synergistic and antagonistic effect of various drugs and to some newer drugs such as mecholyl, prostigmine and furfuryl trimethyl ammonium iodide. The chapter on physical therapy has been brought up to date by including new information on physical and irradiation therapy and on the use of buffer solutions and preservatives for ophthalmic solutions.

Although there are some points on which many ophthalmologists will not agree, notably the injection of cocaine and the treatment of progressive myopia, the book is excellent. It is simply written and well illustrated.

As a book of reference on modern ocular therapeutics, it will be found both useful and interesting. We have great pleasure in recommending it to ophthalmologists and medical men interested in eye work in India.

E. O'G. K.

ANATOMY (THORAX), PART V, CATECHISM SERIES.—By C. R. Whittaker, F.R.C.S.E., F.R.S.E. Fifth Edition. E. and S. Livingstone, Edinburgh. Pp. 76. Price, 1s. 6d.; postage, 2d.

This little volume appears in its fifth edition. The medical books of the catechism series are already familiar with students.

The present volume is improved in having a section on the lymphatic system. The subject-matter has been presented concisely in the form of answers to all important and probable questions bearing on the part.

The student will therefore find it of real help before his examinations when he is confronted with the need for the marshalling of relevant points learnt from massive textbooks; this book will enable him to do so with considerable economy of his time and labour.

S. C. S.

HABIT AND HERITAGE.—By Frederic W. Jones, D.Sc. (London, Adelaide, Melbourne), F.R.S., F.R.C.S. 1943. Kegan Paul, Trench, Trubner and Company, Limited, London. Pp. 100, with 17 illustrations. Price, 5s.

In this small book the writer puts together matter which has formed the subject of various lectures given at various times in varying circumstances. The book, however, shows little sign of this. The line of thought and the presentation are developed consistently in a logical and orderly way.

The main objects of the book are two. The first is to point out that the belief that acquired characteristics are not inherited has led to a lowering of standards and a shrinkage of human spiritual ideals. This idea is explained by the writer as follows:—

'Has not science—even in the most considered and orthodox pronouncements of its most distinguished exponents—possibly led humanity astray in the matter of responsibility in heredity? There was a time when people believed that the sins of the fathers were visited on the children. This belief was incorporated into the teaching that the parents need have some care in their ways of life, lest their acquired shortcomings and moral lapses might be perpetuated in their descendants. It led also to a general belief in the possible ultimate betterment of mankind by a raising of the standard of parental mode of life and well-being. Such hopes have been dashed to the ground. Loud-voiced science has told the people that characters acquired by individuals can under no circumstances be transmitted to their descendants. It matters not if we live good lives or bad, for, apart from direct disease or social degradation, we cannot hand on to our descendants any virtues or vices, any talents or degeneracies that we may have acquired during our lifetime'.

Regarding the old controversy regarding the relative importance of Nature and Nurture the writer states—'To-day, the battle has been won for nature (or genetic constitution) and nurture has ceased to be regarded as being of any importance whatever in the ultimate development of a stock. It is only the germinal constitution—the type and disposition of the hypothetical genes—that counts. If all is well with these, the environment in which the stock happens to find itself makes little or no difference. Conversely, no matter how ideal the environment may be for betterment, it is wasted if the stock that enjoys it happens to be of "inferior" genetic constitution. It is here that the whole thesis has become interwoven with all the mischief wrought by the blind acceptance of the "survival of the fittest" slogans and all that is worst in the modern pseudo-science of race theories. This modern perversion of the science of genetics teaches that a human stock, which, for some reason, is assumed by some people to be fittest, should be bred from as we breed from stud animals in husbandry; and that human stocks adjudged to be less fit should be eliminated. The term "stock" is then translated as "race" and the most dangerous thesis to which real science has even given countenance, and to which pseudo-science has given absolute assurance and practical effect, is begot'.

The writer then goes on to point out that there is considerable evidence that acquired characters may be inherited, and adopts Doncaster's definition of an acquired character as follows 'a feature developed during the life of the individual possessing it, in response to the action of use or environment'.

He devotes twelve pages to an attack of Weismann's theory of the continuity of the germ plasma and points out that much of the evidence on which the theory was based has since been shown to be faulty.

In the following chapter the writer discusses four cases of what appears to be the inheritance of acquired characters. The first is the articular facets produced on the tibia and astragalus in Asiatic people who have the habit of squatting, and the writer points out that these facets are found in young babies long before they have squatted at all. Similar inherited characters are found in the young children of the Australian aborigines, who adopt different methods of squatting. Another example quoted is the downward curve in the cervical region of the vertebral column of the embryonic seal, 'originally acquired' in a long succession of its ancestors in the action of swimming, which has become incorporated into the common heritage of the race.

One chapter is devoted to producing evidence to show that the direction of growth of hair of mammals, which is normally from the nose backwards, has in certain animals been modified by the method of the 'toilet of the coat' adopted by the animal; this changed direction of hair growth is seen in the newborn animal before it has ever scratched itself. The final example is based on the study of the genital organs of the wallaby and cannot be discussed here.

The author considers that these and other examples of inheritance of acquired characters are definitely proved, and thus aims a blow at the doctrine of the non-inheritance of acquired characters and indirectly at the social implications and the racial theories which have been built on this doctrine.

The book is well written and the material and the arguments are excellently presented.

J. L.

Abstracts from Reports

ANNUAL REPORT OF THE UNION MISSION TUBERCULOSIS SANATORIUM, AROGYA-VARAM, NEAR MADANAPALLE, SOUTH INDIA, FOR THE YEAR 1941-42

The sanatorium has now 253 beds. During the year 402 patients were admitted, 412 were discharged, and altogether 667 were treated. By far the largest number had pulmonary tuberculosis. Out of 306 patients analysed in the report, 80 per cent on admission were advanced cases. The results were 'arrested' in 18, 'quiescent' in 25, 'much improved' in 136, 'improved' in 51, 'stationary' in 23, 'worse' in 28 and 'death' in 25.

The sanatorium continued to train doctors and students coming from various places as well as the candidates for the Tuberculosis Diseases Diploma.

The report records with deep regret the resignation of Dr. C. Frimodt-Møller who was intimately connected with the sanatorium since its beginning.

REPORT OF THE KASHMIR MEDICAL MISSION OF THE CHURCH MISSIONARY SOCIETY FOR THE YEAR 1942. MISSION HOSPITAL IN SRINAGAR

The work during the year included district tours, preaching and attention to the sick. A number of villages were visited to come in contact with patients and their friends and to sell gospels. The more serious cases were sent to the hospital. Altogether 27,982 patients were attended, 2,519 were admitted to the hospital, and 4,669 surgical operations were performed.

All who are interested in the work may send their subscriptions or donations to the Mission.

FOURTH ANNUAL REPORT OF THE TUBERCULOSIS ASSOCIATION OF INDIA, NEW DELHI, FOR THE YEAR 1942

The report begins with a tribute to Her Excellency the Marchioness of Linlithgow; her pioneer work will be remembered with great appreciation.

Three new tuberculosis associations were affiliated to the Tuberculosis Association of India during the year thus making a total of 29 existing at present in different Provinces and States. There are now 112 tuberculosis clinics and 66 hospitals and sanatoria in India, with over 4,000 beds. Besides there are 1,207 beds in general hospitals and 737 beds in jail hospitals.

The Lady Linlithgow Sanatorium has made a satisfactory progress during the year, and the New Delhi Tuberculosis Clinic has continued to play an important part in the diagnosis, treatment and prevention of the disease.

A scheme of organized home treatment of tuberculous patients is at hand; annual inspection of school children is undertaken, and educative work is carried out through health visitors. Publicity work was carried out in different provinces. Posters, pamphlets and films were prepared, and a large amount of the material was sold at cost price. Two short post-graduate courses were conducted, one in Patna and another in Lahore.

During the year a standardized classification of pulmonary tuberculosis was published as well as a special tuberculosis number of the *Indian Medical Gazette*. Another publication of the Association was the proceedings of the second Tuberculosis Workers' Conference held in 1940.

Service Notes

APPOINTMENTS AND TRANSFERS

LIEUTENANT-COLONEL F. J. ANDERSON, C.I.E., M.C., I.M.S. (Retd.), Professor of Surgery, Medical College, Calcutta, is appointed to act as Principal, Medical College, Calcutta, in addition to his own duties *vice* Dr. U. P. Basu on leave.

On reversion from military duty Lieutenant-Colonel S. D. S. Grevil resumed charge of the post of Imperial Serologist, Calcutta, with effect from the forenoon of the 15th May, 1943.

INDIAN MEDICAL SERVICE (Emergency Commissions)

To be Major

Narendra Nath Roy. Dated 21st April, 1943.

To be Captains

Mohd. Iqbal. Dated 19th January, 1943.

Abdul Ghani. Dated 15th March, 1943.

Dharma Raj Subramania Iyer. Dated 16th March, 1943.

Mohammed Ishaq. Dated 31st March, 1943.

1st April, 1943

Thota Jagan Mohan Rao.

Kattasomanahalli Venkatakrishnappa Krishnamurthy.

Navaratna Srinivasa Rao.

2nd April, 1943

Hemendra Nath Sen.

Rabindra Narayan Sinha.

H. Padmanabhan.

Santaacruz Thangaraj Arputhraj.

3rd April, 1943

Kallodikuzhil Kochuommen Titus.

Sailes Chakravarti.

Sibabrata Chatterjee.

5th April, 1943

Jaladhi Kumar Sarkar.

Sanatan Nandi.

8th April, 1943

Jayanta Kumar Sen.

Nitya Gopal Roy.

Snubodh Kumar Mukherjee. Dated 12th April, 1943.

Indu Bhushan Sen Gupta. Dated 16th April, 1943.

Archie Norman de Quadros. Dated 21st April, 1943.

Amiya Nath Chakraborty. Dated 22nd April, 1943.

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Chitta Ranjan Chakraverti. Dated 3rd May, 1943.
Kaikhushru Nasarvanji Choksy. Dated 5th May, 1943.

Dhirendra Chandra Banerjee. Dated 6th May, 1943.
7th May, 1943

Oswald John Francis D'Sylva.
Saroj Kumar Biswas.
Sudhansu Kumar Ray Chaudhuri.
Harendra Keshore Verma.
Kambi Siddaramappa Shadaksharappa.
Kailash Narain Tandon.

Kartik Chandra Mukherjee. Dated 8th May, 1943.
Surendra Kumar Chandra. Dated 11th May, 1943.
Kalipada Banerjee. Dated 12th May, 1943.

The undermentioned officers are transferred to the General Service Cadre, with effect from the date specified :—

INDIAN LAND FORCES
(Emergency Commissions)
Captains

C. G. P. Rao. Dated 5th April, 1943.
A. K. Mukerji. Dated 15th April, 1943.
Captain S. R. Chatterji. Dated 19th May, 1943.
Captain D. H. Harrison, Staff Surgeon, Murree, assumed charge of the additional duties of the Civil Surgeon, Murree, on the afternoon of the 24th May, 1943, relieving Major A. V. O'Brien, transferred.

The following transfers are made :—

INDIAN MEDICAL SERVICE—SECONDED TO INDIAN ARMY
MEDICAL CORPS

(Emergency Commissions)
Captains

C. E. Varkkey. Dated 26th March, 1943.
Max Warner Grunstein. Dated 19th December, 1942.
Cyril Gustave Bree. Dated 16th May, 1943.
Ignatius James Yu-Chieh Hsu. Dated 21st January, 1943.

23rd February, 1943

Alen Rex Adderley.	Harry Lipman.
Edward John Rubra.	Keith Alexander Swales.
Roy MacGregor McGowan.	James Wright Anderson Crabtree.

Owen Sookias.

INDIAN ARMY DENTAL CORPS

(Emergency Commissions)

To be Captains

5th May, 1943

George Mathias.
Lekh Raj Bhalla.
Nariman Rustonji Vazifdar.
Sorab Munchershaw Nicholson.
Mohan Dev Mehra.

6th May, 1943

Hari Dayal Gupta. Keshab Chandra De.
Harish Chandra Aurora. Dated 7th May, 1943.

To be Captain for service with Royal Indian Navy
Prasanna Kishore Nawal Kishore. Dated 1st June, 1942.

INDIAN MEDICAL SERVICE—SECONDED TO INDIAN ARMY
MEDICAL CORPS

(Emergency Commissions)

The undermentioned officers are transferred to the General Service Cadre, with effect from the date specified :—

Captains

B. R. Mahajan. Dated 26th April, 1943.
A. K. Ghosh. Dated 2nd May, 1943.

Lieutenant

S. K. Das. Dated 12th May, 1943.

(Emergency Commissions)

To be Lieutenants

Colin Weston McNamara. Dated 3rd January, 1943.
Samuel McClatchie. Dated 23rd January, 1943.
Cecil Joseph Pereira. Dated 7th April, 1943.

Leslie George Raworth Hull. Dated 4th May, 1943.
Samuel Clifton Macmillan. Dated 27th April, 1943.
George Skinner. Dated 11th May, 1943.
Maurice Edmund Tapissier. Dated 11th May, 1943.
Archibald Joseph Ralston. Dated 4th November, 1942.

Kapil Deva Malaviya. Dated 6th March, 1943.
Akhtar Hussain Awan. Dated 8th March, 1943.
Kamala Patricia Roe. Dated 13th March, 1943.
Bibhas Chandra Mitra. Dated 8th April, 1943.
Purnendu Bikas Roy. Dated 15th April, 1943.
Basil George Bamford. Dated 19th April, 1943.
Reginald Paul Harvey. Dated 21st April, 1943.

8th May, 1943

R. Narayanan.
Tiruvarur Sundaresa Ramaratnam.
Gopala Krishnamurthy Atuluri.
A. J. Arunagiri.
Coilore Ramiah Suryanarayan.
Pannimadai Vaidiswaran Krishnamurti.
B. V. Rama Rao.

John Charles Allan Dique. Dated 14th May, 1943.

To be Captain for service in the Royal Indian Navy

Sarosh Bhacca. Dated 5th May, 1943.

To be Captains for service in the Indian Air Force

Holavanahalli Anandarao Nagaraja Rao. Dated 20th March, 1943.

Chathapuram Ramayyar Krishnamurthy. Dated 9th April, 1943.

To be Lieutenants for service in the Indian Air Force

Wizarat Ullah Khan. Dated 8th March, 1943.

Arun Kumar Basu. Dated 15th March, 1943.

Gobichettipalayam Nageswara Iyer Venkatraman. Dated 20th March, 1943.

(WITHIN INDIAN LIMITS)

To be Captains

Lakshimpuram Sreenivasiengar Doraswamy. Dated 2nd April, 1943.

7th May, 1943

Tincouri Dey. Nilakanta Vythianathan.
Bharthur Alasingrachar Sreenivasaiyengar. Dated 8th May, 1943.

(WOMEN'S BRANCH)

To be Captains

(Miss) Jaul Barjorji Hakim. Dated 11th March, 1943.

(Miss) Siloo Sorabji Daruvala. Dated 15th April, 1943.

(Miss) Jacinth Muriel Gaudoin. Dated 19th April, 1943.

(Miss) Winifred Agnes Vaz. Dated 19th April, 1943.

To be Lieutenants

(Miss) Eileen Saraswati Chaube. Dated 20th March, 1943.

(Miss) Sushila Devi Chopra. Dated 12th April, 1943.

PROMOTIONS

INDIAN MEDICAL SERVICE—SECONDED TO INDIAN ARMY
MEDICAL CORPS

Majors to be Lieutenant-Colonels

S. P. Joshi. Dated 25th May, 1943.

R. Linton. Dated 29th May, 1943.

H. W. Mulligan. Dated 29th May, 1943.

Major A. N. Chopra is granted the local rank of Lieutenant-Colonel, without effect on pay and pension, whilst employed as Director of Health and Inspector-General of Prisons, Orissa. Dated 25th May, 1943.

INDIAN LAND FORCES

INDIAN MEDICAL SERVICE—SECONDED TO INDIAN ARMY
MEDICAL CORPS

(Emergency Commissions)

Captains to be Majors

V. D. Nimbkar. Dated 16th April, 1943.

S. N. Aggarwal. Dated 14th May, 1943.

INDIAN MEDICAL SERVICE

Captains to be Majors

B. N. Bhandari. Dated 21st May, 1943.
 M. N. Mahmood. Dated 22nd May, 1943.
 B. L. Kapur. Dated 22nd May, 1943.
 P. M. Kaul. Dated 26th May, 1943.
 A. K. Dev. Dated 31st May, 1943.
 M. Akram. Dated 2nd June, 1943.

INDIAN LAND FORCES

INDIAN MEDICAL SERVICE—SECONDED TO INDIAN ARMY
MEDICAL CORPS*(Emergency Commissions)**Captain to be Major*

R. U. Qureshi. Dated 1st March, 1943.

Lieutenants to be Captains

3rd May, 1943

A. Peters. T. H. E. H. Gnanaiya.
 H. D. Messiahdas. Dated 4th May, 1943.

8th May, 1943

N. Chondhuri. B. Mukerjee.

A. K. Basu.

B. K. Mukherji. Dated 13th May, 1943.

15th May, 1943

Abdul Karim.	W. M. S. Jonas.
S. Lile.	N. R. Ramakrishnan.
S. I. R. Sarma.	E. J. D'Netto.
K. Umapathi.	V. P. Rangaswami.
R. Rajagopalan.	V. Selvaraj.
J. Srinivasan.	S. Krishnan.
S. R. N. A. Babu.	R. R. Rao.
T. M. Seethapathy.	A. P. Babu.
K. C. Ganapathy.	M. Rahimulla.

16th May, 1943

A. Shetty.	S. P. Vedachalam.
E. P. Gonsalves.	D. A. Narasimhan.
P. S. Selra. Dated 17th May, 1943.	
S. M. M. Razvi. Dated 26th May, 1943.	
S. H. Massey. Dated 27th May, 1943.	

28th May, 1943

P. P. Balakrishnan. P. V. Rao.

B. G. Achar.

M. P. Jesudasan. Dated 30th May, 1943.

LAND FORCES—INDIAN MEDICAL SERVICE

*(Emergency Commissions)**Lieutenants to be Captains*

J. F. Cameron. Dated 18th October, 1942.

25th November, 1942

J. M. Murray.	R. Gardiner.
G. McCracken.	A. G. Hick.
R. M. Craig.	A. G. Doughly.
D. A. K. Carnegie. Dated 10th February, 1943.	
M. W. Grunstein. Dated 25th November, 1942.	
N. V. Nene. Dated 4th March, 1943.	

INDIAN LAND FORCES

INDIAN MEDICAL SERVICE—SECONDED TO INDIAN ARMY
MEDICAL CORPS*(Emergency Commission)**Lieutenant to be Captain*

Hasan Din. Dated 6th March, 1943.

LAND FORCES

INDIAN MEDICAL SERVICE

*(Emergency Commissions)**Lieutenants to be Captains*

11th May, 1942

G. R. Butterfield.	A. C. Greene.
G. Barwell. Dated 10th July, 1942.	
C. Sonick. Dated 25th July, 1942.	
W. M. Doolin. Dated 25th September, 1942.	
A. E. Fraser-Smith. Dated 4th December, 1942.	

LAND FORCES

INDIAN MEDICAL SERVICE—SECONDED TO INDIAN ARMY
MEDICAL CORPS*(Emergency Commission)**Lieutenant to be Captain*

R. H. Vasey. Dated 28th May, 1941.

*Lieutenants (on probation) to be Captains
(on probation)*

D. J. Gilbert. Dated 5th November, 1941.

N. K. Woll. Dated 24th November, 1942.

(Miss) E. Heath. Dated 16th January, 1943.

21st February, 1943

(Miss) E. E. G. Baillie. (Mrs.) E. C. Just.
 (Miss) E. G. Fisher.

(Miss) H. Billig. Dated 10th April, 1943.

RETIREMENTS

Colonel C. A. Wood, M.C., K.H.P. Dated 16th May, 1943.

Lieutenant-Colonel A. Chand. Dated 21st November, 1942.

Lieutenant-Colonel G. Verghese, C.I.E. Dated 9th June, 1943.

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Original Articles

ON THE CARDIAC EFFECTS OF EMETINE*

By ROBERT HEILIG, M.D.

and

S. K. VISVESWAR, M.B., B.S.

(Krishnarajendra Hospital and Medical College,
University of Mysore)

It is a curious fact that no agreement exists in literature about the frequency and extent of untoward cardiac by-effects of emetine and even about the best way of administering emetine. Brown (1935) studied a large number of cases of amœbiasis treated with emetine, and thought that real cardiac damage was very rare; the circulatory changes he attributed mainly to vasomotor affection. Chopra (1934), Mackie (1936) and others warn against its use in the presence of myocardial lesions and other organic heart diseases. This question is of great practical importance, because, if the latter opinion were justified, we would find hardly a case where emetine could be used safely, most of our cases of amœbic dysentery showing some sign of heart-muscle damage, due to a co-existent hookworm infection, to chronic malaria, or to the dysentery itself. That some difference of opinion exists about the best way of emetine application—whether by the intramuscular or intravenous route—is shown by the attitude of the authoritative textbooks. Strong, the editor of Stitt's 'Textbook of Tropical Diseases' (1942), simply states: 'intravenous injection should not be employed'. Manson-Bahr (1941) declares: 'emetine must be given subcutaneously or intramuscularly. It is a toxic drug, especially to children and women, when given *intravenously*'. In strict contradiction to this teaching, Muehlens *et al.* (1938) say: 'emetine hydrochloride is injected subcutaneously (causing infiltrations), intramuscularly or *intravenously*. We always preferred the latter way of application' (translation).

We have therefore tried to collect material bearing on the two main questions: (1) whether emetine, administered by the intramuscular route, in therapeutic doses causes cardiac damage so frequently and to such an extent that it has to be used with special care or not at all, if some cardiac lesion is present; (2) whether a significant difference exists between the cardiac by-effects of intramuscular and intravenous emetine administration in man. To achieve these purposes the following investigations have been performed.

Forty-five unselected patients with acute amœbic dysentery, ten of them women, received

a course of twelve emetine injections, one grain per day, the course consisting of two lots of six injections with one day's interval. To fourteen of these patients, emetine was given by the intramuscular route, and electrocardiograms were taken before the first, after the sixth, and again after the twelfth emetine injections; at the same time an orthodiagram was traced and the blood pressure was estimated. Thirty-one patients, six of them females, received the same amount of emetine within the same time by the intravenous route. In sixteen of these thirty-one cases, electrocardiograms were taken and blood pressure was estimated before and at various intervals (up to one hour) after the first and second, sixth or twelfth emetine injections; in the other fifteen cases the blood pressure was measured, and cardiograms and orthodiagrams were taken before the first and after the sixth and twelfth grain of emetine; moreover, in most of them, the cardiograms were traced at all the three stages of the emetine course before and after exertion, which consisted in climbing thrice up and down 29 steps at maximum speed. As a matter of course the standardization of the cardiograms was kept constant.

Out of the fourteen patients who received emetine by the *intramuscular route*, eleven had a pathological cardiogram before the treatment started, and three were normal. These pathological findings consisted in low voltage, flat T-waves, or—rarely—in a depressed S-T. During the treatment of the three normal cases, one remained uninfluenced, one developed a slightly higher P_2 , T_1 and T_2 as the course progressed, and one became worse as far as the cardiogram was concerned. Altogether the following changes, manifested in the cardiograms, accompanied the intramuscular emetine application: some improvement was achieved in eleven out of fourteen cases; no change was seen in two; and some deterioration occurred in one initially normal case (see figure 2, plate XXI). This last patient (case 26), an emaciated Hindu ryot, 35 years old, remained febrile and continued passing dysenteric motions up to the tenth emetine injection; accordingly the cardiogram (figure 2b) taken after six grains showed a worse myocardial condition than that at the beginning of treatment (figure 2a), whereas the third one (figure 2c), traced after 12 grains, was better than the second, but still not as good as the first, as far as the voltage of all the leads and T_2 were concerned.

Figure 1 (plate XXI) reproduces the cardiograms of one of the eleven cases, in which, along with the clinical improvement of the intestinal condition, the cardiogram approached the normal. Before emetine, figure 1a shows an extremely low R in all the 4 leads; T_1 is iso-electric and T almost absent in the 3 other leads. After six grains of emetine (figure 1b) R_2 and R_4 are higher and so are the T-waves in all the 4 leads; a further increase of R_1 , R_4 and T_1 appears after twelve injections (figure 1c) when

* A discussion of this subject appears in the editorial section of this number.—Editor, I. M. G.

also the previously downwards convex S-T₄ becomes perfectly normal.

Because of Mackie's (*loc. cit.*) warning against any emetine medication in organic heart disease, the following case deserves to be specially mentioned. A Mohammedan girl, 12 years old (case 23), showed, before emetine treatment was started, an incomplete heart block (figure 3a, plate XXI); the conducted beats had an enormously prolonged P-R interval of 0.40; after a varying number (figures 1 to 3) of conducted sinus beats, either a blocked P or a ventricular extra-systole appeared, originating from the apical part of the right ventricle. After six intramuscular emetine injections, an absolutely regular sinus rhythm was established; long tracings of the cardiogram still showed a prolonged conduction time, but apparently all beats were conducted and not a single extra-systole appeared (figure 3b); whether blocked P-waves are completely hidden in T could not be decided. After 12 grains of emetine the picture changed to a regular 2:1 block with the blocked P-waves clearly visible in the T-waves and P-R reduced to 0.20 in lead I. The general and, especially, the circulatory condition was incomparably better after the emetine course than before.

In this group, the blood pressure varied only slightly. Between the first and sixth injection usually a fall of 5 to 8 mm. Hg. systolic, never exceeding 10 mm., was recorded, whereas the diastolic pressure simultaneously was diminished by not more than 5 mm. During the second half of the course, the initial pressure was frequently restored.

The orthodiagrams did not show any significant change of size and shape of the heart outline.

After intravenous emetine injections the cardiographic changes show a wider range of variation. In none of these thirty-one cases, of which only eight had a normal cardiogram on admission, did an irregularity of the heart rhythm appear; no extra-systoles, no block and no auricular fibrillation developed during the treatment.

Sixteen patients have been tested in 'short-range' experiments, cardiograms having been taken before the first intravenous injection of one grain of emetine, and 5, 15, 30 and 60 minutes afterwards; or before and 15 minutes after the first, second, sixth or twelfth intravenous emetine injection. Among these subjects, four had a normal cardiogram when treatment was started; within one hour all these four cases showed some deterioration under the influence of emetine. Out of five women included in this series, all of whom presented some pathological cardiographic signs on admission, four remained unaltered after emetine.

The total result of the immediate experiments is that in the course of intravenous emetine medication under the described con-

ditions, no definite changes have been noticed in ten out of sixteen cases. In the remaining six the following alterations occurred. A prolongation of P-Q was seen twice, from 0.16 to 0.18 and from 0.15 to 0.19 seconds respectively; the voltage of R in one or more leads was diminished in three cases, and the T-waves in one or more leads were flattened in five cases; an increased notching of R_s was noticed once. In one case, a woman, T₁ and T₂ appeared slightly higher 15 minutes after the first injection, an effect which subsided after one hour.

The two cases of delayed conduction occurred after the first injection in previously normal cardiograms; diminished voltage was observed twice after the first, once after the sixth injection; lowered T-waves appeared twice after the first, three times after the sixth administration.

The blood pressure changes have been recorded in almost every case; they were independent of electrocardiographic findings. As early as 10 to 15 minutes after the first intravenous injection, both the systolic and diastolic readings were diminished by 5 to 10 mm. Hg.; they usually remained constant for the next hour, though in two cases a further reduction of the systolic pressure by about 10 mm. occurred, whereas the diastolic remained unaltered.

Figure 4a and figure 4b (plate XXI) show the cardiograms of a Hindu ryot, 22 years old, traced before and 15 minutes after the first injection; figure 4c and figure 4d show those made before and 15 minutes after the sixth grain of emetine in the same case, which presented a normal cardiogram at the outset. After the first injection, in lead I, P-Q increased from 0.15 to 0.19 second, and R_s decreased in height; after the sixth injection the changes are certainly not more extensive, although the cardiogram taken before this injection (after giving five grains of emetine on the five preceding days) shows a distinct flattening of T₁, T₂ and T₄ as well as an almost complete disappearance of P₂. The blood pressure, estimated before the first injection, was 120/80; 15 minutes after the intravenous injection of the first grain of emetine 116/72 mm. Hg., before the sixth injection it was 104/60 and remained so 15, 30 and 60 minutes afterwards.

On the other hand, patients showing considerable myocardial lesions prior to emetine medication, did not suffer any deterioration following the first and sixth injection (figure 5, plate XXI).

In the last group, comprising fifteen cases, the same investigations as were performed in the previous groups were repeated under the influence of exertion; an electrocardiogram was taken and the blood pressure estimated before and immediately after exercise (climbing thrice up and down 29 steps) before the first, after the sixth and after the twelfth intravenous emetine injection; this method was employed to detect functional changes which might escape our notice if the patients are examined only at rest.

Orthodiagrams have been traced at the same three stages of the treatment. Before the onset of emetine medication, four of these test subjects had a normal cardiogram, which in three of them showed some deterioration during the course of intravenous injections, whereas in one case, after a slight flattening of T_1 at mid-course, the voltage of R_1 and R_2 considerably increased by the end of treatment. Summing up the results obtained in these fifteen cases we find a diminished height ('voltage') of R in six cases, in three after the sixth and in three after the twelfth grain of emetine; an increased 'voltage' was found once after the sixth and once after the twelfth injection. A lowering of T in one or more leads became manifest in nine cases, in three after six and in six after twelve grains; in one of them, T_2 and T_3 , in three others T_4 became inverted. In five cases the height of the T -waves increased after six injections, an improvement which was maintained up to the end of the course in three patients. Thus, no change occurred in one, some deterioration was found in nine, and some improvement in five cases. It is noteworthy that none of the myocardial lesions which appeared during the treatment was brought to light by the exertion test; all of them already were manifest at rest and were merely accentuated by exertion.

Figure 6 (plate XXI) shows the cardiograms of a Hindu female, 40 years old; on admission the rest cardiogram (figure 6a) showed a low T_2 and an isoelectric T_3 ; after exertion T_2 almost disappeared, T_3 became inverted, and the 'voltage' of R_4 diminished, in spite of an uneventful afebrile clinical course of the dysentery, the motions having become normal after three intravenous emetine injections of one grain each; the cardiographic tracings after six grains (figure 6b) presented a still flatter T_2 , a reduced R_3 , an inverted T_3 and lower T_4 , signs of increased myocardial damage which became still more marked after twelve grains (figure 6c), when T_2 appeared slightly inverted, T_4 biphasic, and R_4 disappeared completely.

Figure 7 (plate XXI) depicts the cardiograms of a Hindu male, 22 years of age; before emetine treatment was started (figure 7a) T_2 was almost isoelectric, T_3 inverted; in figure 7b, taken after six intravenous injections of one grain each, R_1 , R_2 and T_4 were higher and T_2 became distinctly positive. Finally (figure 7c), after twelve grains of emetine, R_1 and T_1 were twice as high as before medication, T_2 was perfectly normal and T_4 increased from 4 to 10 mm. The tracings after exertion are almost identical with those reproduced here. The blood pressure on admission was 112/80; after six and twelve injections 105/75. The orthodiagram showed a slight reduction of the transverse diameter, due to a straightening of the right auricular outline.

Figure 8 (plate XXI) illustrates one of those two cases in which a considerable improvement took place during the first half of the course, whereas—in spite of a steadily maintained

clinical progress—the last cardiogram (after 12 grains) showed a reversion to the initial condition. The reproduced cardiograms are the tracings of a Hindu male, 38 years old. On admission (figure 8a), R_4 was low, T_2 absent and T_3 inverted; after exertion R_1 , T_1 and T_4 increased, $S-T_2$ was depressed. At mid-course (figure 8b) R_4 , T_2 , T_3 and T_4 became higher; after exertion T_2 and T_3 lower. After twelve intravenous injections (figure 8c) again T_2 was isoelectric, T_3 slightly inverted and T_4 much lower than in figure 8b; exertion bent $S-T_2$ downwards.

Discussion

Apparently, there is no divergence of opinion about the cardiac action of emetine in experimental animals; an overdose causes ventricular fibrillation in rabbits which, however, does not exclude the possibility of recovery (Levy and Rowntree, 1916). The electrocardiographic changes caused by acute emetine intoxication in cats have been analysed by Boyd and Scherf (1941), who found a delayed conduction, the appearance of extra-systoles, etc., following intravenous application. Emetine was even used in a routine way to produce a damaged myocardium for experimental purposes (Hein and Vannotti, 1939). The microscopic pathology of the heart in emetine intoxication was worked out by Chopra *et al.* (1924), who found degenerative changes in rabbits, by Rinehart and Anderson (1931), who described histological findings in the myocardium of the same animal resembling those seen in rheumatic fever, and Epstein (1932), who reported myocardial degeneration up to necrosis as a characteristic feature. Less unanimity is to be found in the literature on toxic cardiac by-effects of therapeutic emetine doses in man. As pointed out in our introductory remarks, Chopra (*loc. cit.*) and Mackie (*loc. cit.*) would confine the use of emetine to persons with a sound myocardium, and Sellard's (Strong, 1942) cautions against its further application in such cases where a fall of blood pressure was recorded. On the other hand, Brown (*loc. cit.*) doubts whether untoward cardiovascular reactions are frequently seen, none having occurred in 554 cases of amoebiasis in fifteen years of clinical experience at the Mayo Clinic; the average total dose used there was ten grains, injected subcutaneously. Among the twenty cases of emetine poisoning collected by Levy and Rowntree (*loc. cit.*), none is tabulated with the manifestation of cardiac symptoms. And, yet, emetine is supposed to be a cardiac depressant (Chopra and Chopra, 1942), the use of which should be limited to a minimum. This opinion seems to be based on the results of animal experiments on the one hand and on a few cases of cardiac damage, reported in detail, on the other hand. Craig's (1936) statement that he 'has observed several cases in which death from myocarditis or from sudden cardiac failure was apparently caused by excessive dosage with emetine' is too vague

to be discussed, though this author's wide experience on amœbic infections carries great weight. The cardiograms of the cases of cardiovascular reaction reported by Anderson and Reed (1934) do not prove a definite myocardial lesion; such effects could be of vagal origin. The case described by Chopra and Sen (1934) had received emetine-bismuth-iodide a few months prior to the course of emetine injections, quinine and digitalis just previously to tracing the cardiogram which is reproduced and, moreover, no cardiogram was taken, permitting comparison, before emetine treatment was commenced. In Sayid's (1935) two cases of auricular fibrillation, supposed to be the result of emetine, no cardiograms were traced and one of them was suffering from a mitral valvular lesion in the course of which auricular fibrillation might start at any time. We have found no other case reports of cardiovascular damage caused by emetine in the literature at our disposal.

Our own investigations seem to prove that twelve grain courses of emetine, given in doses of one grain by the intramuscular route, have no damaging effect on the myocardium even if there is some myocardial defect at the commencement of this medication, such as was the case in eleven of our patients. Moreover, in eleven out of fourteen cases, the cardiograms showed that some improvement of the myocardial condition developed during the emetine course and was maintained up to the end of it. The only patient who suffered some deterioration was the only one whose dysentery did not respond promptly to the treatment. The explanation of these observations seems to be that the positive effect upon the heart, exerted by the improvement of the intestinal and general condition under the influence of emetine, prevails over a possible negative emetine effect on the heart muscle. There is no doubt that amœbic dysentery increases the permeability of the colonic mucosa to such an extent that an amount of intestinal toxins—though not of amœbic origin—sufficient to damage the myocardium enters the circulation. That even serious muscle damage is not a strict contra-indication against the use of emetine in reasonable dosage is proved in our case of an incomplete auriculo-ventricular block with ventricular extra-systoles, which improved during the course of emetine.

On the other hand, the results of intravenous emetine administration confirm the fact, proved up to now only in animal experiments, that by exceeding a certain emetine concentration, either in a single dose or by cumulative action, signs of a myocardial lesion could be produced. Acute effects of intravenously injected emetine, appearing within 15 to 60 minutes, were observed in six out of sixteen cases but their extent was by no means alarming. A delayed conduction, which still remained within normal limits, found in two cases, a slightly diminished voltage in three, and a moderately lowered T in five patients, was all the damage done by single

intravenous emetine injections. Whenever the observation was continued up to one hour after the injection, most of the changes, which usually became manifest after 15 minutes, had disappeared by this time. That the individual susceptibility to the drug has more influence on the response than the objective muscle condition is illustrated by our experience that all the four cases which showed a normal cardiogram before the first injection developed some signs of myocardial depression, whereas eight cases with a low initial condition escaped the acute toxic effect, one of them with a serious heart-muscle lesion (figure 5), manifested by splitting and notching of R, a considerable depression of S-T, and an isoelectric or biphasic T in all the leads; and such a heart stood twelve grains of emetine, injected intravenously, without presenting any signs—clinically or cardiographically—of a further damage, the blood pressure falling from 120/50 to 110/46, 7 minutes after the first, and being still 100/40 mm. Hg. after the twelfth injection. It is remarkable that no cumulative effects have been noticed in 'short-range' experiments; the changes which appeared within one hour following the sixth or twelfth grain of emetine have not been more pronounced than those appearing shortly after the first grain in the same case (figure 4, plate XXI), although the cumulative action was well marked when comparing a later eardiogram with an earlier one in those cases in which deterioration did occur.

Turning to the changes in the last group (15 cases) which comprises the investigations performed before and after exertion at the beginning, the middle and the end of an emetine course, administered by the intravenous route, we find a much higher percentage of unfavourable results. Nine cases, i.e. 60 per cent, showed some signs of a myocardial depression, which usually was visible after the sixth and became more marked after the last injection; inversion of T-waves never appeared before the end of the course, which illustrates the cumulative effect of emetine. That the cumulative effect is even capable of overcoming an initial improvement is proved by the two cases which showed some increase of voltage and T after six, and a definite reversion to the pre-emetine condition after twelve grains of emetine (figure 8, plate XXI). The improvement during the first half of the course certainly was due to the same mechanism as in the cases treated by the intramuscular route, to the healing of the bowel affection; whereas the reversion to the initial stage, in spite of clinical progress, was caused by the cumulative effect of emetine. Compared with the improvement which was found in 78.5 per cent of cases treated by the intramuscular route, these results appear still more significant. But judgment against the intravenous administration becomes somewhat less definite when the following facts are taken into consideration. Against some myocardial damage in nine cases,

equally marked improvement was observed in five patients, although they were maintained only in three of them. Unfortunately, it was impossible to keep a sufficient number of our patients long enough—due to scarcity of beds—to find out how long the depressant effect upon the myocardium remains traceable. In two of our cases, re-examination after 17 and 19 days respectively showed previously diminished 'voltage' and lowered T restored to normal. Exertion, imposed upon the patients during and by the end of intravenous emetine therapy, did not bring to light any functional insufficiency of the heart. The cardiograms traced immediately after climbing of 87 steps (three ascents of the staircase leading from the ground floor to the first floor of the hospital) at maximum speed hardly exhibited any significant changes when compared with the curves taken before exertion; in no case did a definite depression of S-T, an inversion of T or a delayed conduction become manifest; signs of deterioration which were present in the resting cardiogram such as a diminished 'voltage' or a lowered T, occasionally became more pronounced, but they were never elicited by exertion, and in the majority of cases no significant difference was found between rest- and exertion-cardiograms (at the same stage of treatment).

The pulse rate remained constant in the immediate experiments, and during the emetine course varied mostly according to the cardiographic changes; a moderate acceleration was noticed when the myocardial condition deteriorated, a moderate slowing down occurred in the patients where the cardiogram improved; no irregularity ever appeared.

The behaviour of the blood pressure is no indicator of a toxic emetine effect, provided that the cardiogram is recognized as a reliable mirror of the myocardial condition. A fall of the systolic pressure was regularly noticed, beginning 5 to 10 minutes following an intravenous injection, whether a change appeared in the cardiogram or not. A moderate reduction of the systolic pressure, not exceeding 10 mm. Hg., was found in most of the patients whose cardiogram improved along with intramuscular emetine medication. More pronounced, rarely amounting to 20 mm. systolic, was the fall during the courses of intravenous injections, but even here the variations did not show any relation to the cardiographic changes; whether improvement or deterioration was seen in the curves, the extent to which the blood pressure sank was practically the same. The average changes of the diastolic pressure were much less; with reductions of the systolic reading up to 10 mm. frequently the diastolic remained constant, thus showing a diminished pulse pressure. These observations and the fact that the pressure alterations do not correspond to a cumulative emetine effect, the pressure reaching its minimum usually before the sixth injection and sometimes

rising again before the twelfth, make it probable that the fall of blood pressure is not due to an impaired heart muscle but to some vasomotor factor; whether the cause of it is to be found in the vasomotor centres, the peripheral circulation or in the influence of emetine on the endocrines (Chopra, Gupta and Roy, 1935) has to be further investigated.

Changes of size and shape of the heart, such as are to be seen in carefully traced orthodiagrams, have been negligible in the course of intramuscular as well as intravenous emetine administration; this fact conforms well to the other clinical findings.

It is not within the scope of the present report to give a detailed clinical account of our observations. It has however to be mentioned that neither in any of the forty-five test subjects included in this series nor in any other of a great many cases treated in our wards with emetine given by the *intravenous* route has any clinical indication of a toxic reaction been observed. Kept strictly in bed (except for the exertion tests), not a single case suffered from nausea, vomiting or toxic diarrhoea, from neuritis or muscular weakness, from urticaria or hæmorrhagic eruptions; neither palpitation nor oppression, neither dyspnoea nor any other circulatory symptom ever was complained of by our patients. After three or four intravenous injections they demanded more food, their diet consisting of whole wheat congee, buttermilk and plantains. It is possible that these favourable results are partly due to the absence of toxic contaminations (cephaline) in the brand of emetine which is used in our hospital. The experiences with emetine injected intramuscularly are equally good as far as the absence of toxic symptoms is concerned; but the pain which so frequently accompanies this form of application makes it sometimes difficult to persuade the patients to take the full course of twelve grains which is necessary—in our opinion—for achieving optimum results. Moreover, the correction of the bowel action and condition of the motions require more time than under intravenous administration. We are unable to state how many of our patients are 'cured', a regular following up of them being impossible; but, whereas the majority of those treated for chronic cardiac or pulmonary diseases, for chronic malaria, arthritis, etc., invariably return to the hospital, we hardly remember a case of amœbic dysentery which was re-admitted with the same complaints within the last three years.

Conclusions

Out of forty-five cases of acute amœbic dysentery analysed in this report, eleven had a normal and thirty-four a pathological cardiogram on admission. During a course of twelve emetine injections of one grain each, nine of the initially normal cardiograms showed some deterioration, whereas a high percentage of the previously pathological tracing improved.

Thus, a moderate myocardial lesion is no contra-indication to emetine therapy.

Intramuscular emetine medication was accompanied by some improvement of the heart-muscle condition in eleven, i.e. 78.5 per cent of fourteen cases.

Intravenous emetine injections caused some deterioration of the cardiograms within one hour following the injections in six, i.e. 37.5 per cent out of sixteen cases. No cumulative effect was noticed in these immediate experiments. During the full course (12 grains) of emetine given by the intravenous route, some myocardial damage, manifested by cardiographic signs, occurred in nine, i.e. 60 per cent of fifteen cases, and some improvement in five, i.e. 33 per cent of the same group.

No significant changes of size and shape of the heart have been seen in orthodiagrams.

Blood pressure changes appearing during emetine treatment are not related to the condition of the heart; a fall of pressure is no sign of a toxic action upon the myocardium.

Intramuscular as well as intravenous administrations of emetine have their advantages; from the point of view of cardiac protection the intramuscular route is safer.

Our thanks are due to Dr. J. F. Robinson, B.A., M.D., F.A.C.S., F.R.C.S.E., Medical Officer, Krishnarajendra Hospital, and Principal, Medical College, for the keen interest he took in these investigations, and to Dr. Mohamed Aga, assistant to our radiologist, for having traced the orthodiagrams.

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MADLUNG'S DEFORMITY: TYPICAL AND REVERSE TYPE

(WITH A CASE REPORT)

By MADAN LAL AGGARWAL, M.B., B.S.
Lahore

MADLUNG'S deformity is an idiopathic progressive condition in which there is dorsal (with anterior concavity) and lateral curvature of the radius, posterior dislocation of the lower end of the ulna, and adduction of the hand due to disturbances of growth at the lower end of the radius. On account of the dorsal curvature with an anterior concavity, the hand is carried on an anterior plane, giving the appearance of a bayonet to the lower part of the forearm (bayonet deformity).

Sometimes the curvature takes place in the reverse direction, i.e. anteriorly with a posterior concavity. In this condition the lower end of the ulna is dislocated anteriorly, and the hand is carried on a posterior plane giving the appearance of a silver fork to the limb (silver fork deformity). This is called the reverse type of Madlung's deformity.

This condition is a distinct clinical entity. Very few textbooks mention this condition, and

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KEY TO PLATE XXI

Intramuscular injections of emetine

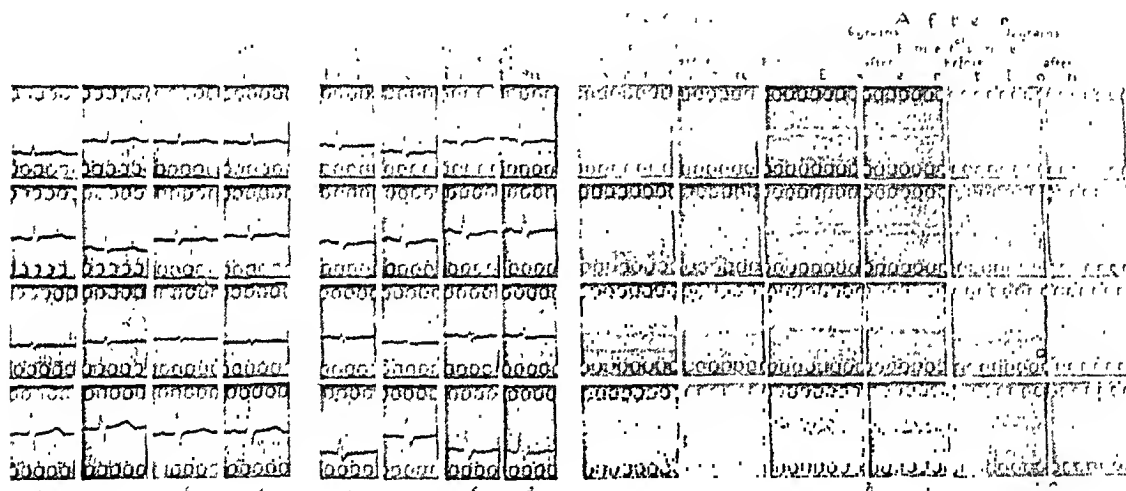
- Fig. 1.—(a) $R_{1,2,3,4}$ very low; $T_{1,2}$ almost absent; S-T₂ downwards convex. (b) $R_{2,3,4}$ higher; $T_{1,2}$ higher. (c) $R_{1,2}$ higher; $T_{1,2}$ normal; S-T₂ normal; well improved.
- Fig. 2.—(a) T_2 low; T_3 inverted; otherwise normal. (b) $R_{1,2,3}$ lower; $T_{1,2,3}$ lower; S-T₂ depressed. (c) Voltage improved; T_2 higher; T_3 inverted; deterioration due to persistent dysentery.
- Fig. 3.—(a) P_1 blocked sinus beat; P-R 0.40 sec.; RS extrasystole. Regular bradycardia; P covered in T? (c) Every alternate sinus beat blocked; no extrasystoles.

Intravenous injections of emetine

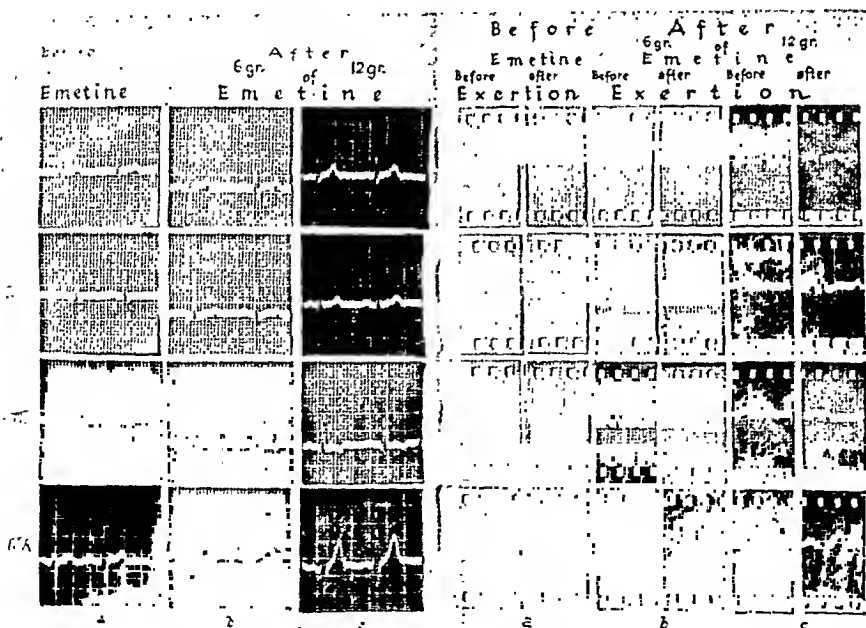
- Fig. 4.—(a) Normal cardiogram. P-Q 0.15. (b) P-Q 0.19; T_2 lower. (c) P_2 almost absent; P-Q 0.16; R_2 , $T_{2,3,4}$ lower. (d) P-Q 0.19; no further deterioration.
- Fig. 5.—(a) Notching or splitting of $R_{1,2,3}$, S_1 ; S-T depressed in all leads; $T_{1,2}$ biphasic. (b), (c) and (d) No further changes.
- Fig. 6.—(a) Normal cardiogram before exertion; T_2 lower; T_3 inverted after exertion. (b) $R_{1,2,3}$ lower; $T_{1,2,3}$ lower; T_3 inverted; $T_{2,4}$ lower after exertion. (c) R_4 almost absent; S-T₄ downwards convex; T_4 biphasic.
- Fig. 7.—(a) T_2 almost iso-electric; T_3 inverted. (b) R_4 , T_3 , T_4 higher. (c) $R_{1,2,3,4}$, $T_{1,2,3,4}$ considerably higher.
- Fig. 8.—(a) $T_{1,2}$ almost absent; T_3 inverted. (b) R_4 , $T_{2,4}$ higher; T_3 low. (c) Reverted to (a).



Figs. 1, 2 and 3.



Figs. 4, 5 and 6.



Figs. 7 and 8.



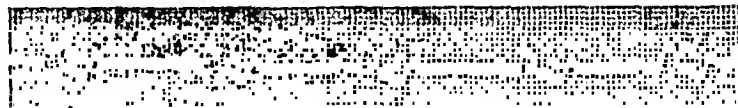
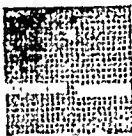
Fig. 2.—*Left* : Triangular lower radial epiphysis, absence of epiphyseal line on the medial side, zone of rarefaction and lateral curvature of the radius. *Right* : Large and irregular lower radial epiphysis, zone of rarefaction and bony excrescence.



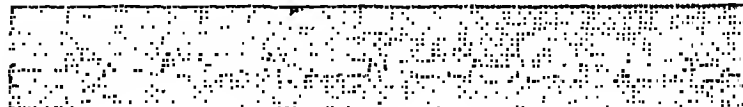
Fig. 3.—*Left* : Hand at posterior plane, dinner-fork deformity, anterior curvature of the radius and anterior dislocation of lower end of ulna. *Right* : Hand at anterior plane, bayonet deformity, anterior bending at the lower end of the radius, fusion of the radial epiphyseal line anteriorly and posterior dislocation of lower end of ulna.

HYPERSENSITIVITY OF THE CAROTID SINUS : L. B. CARRUTHERS. PAGE 426

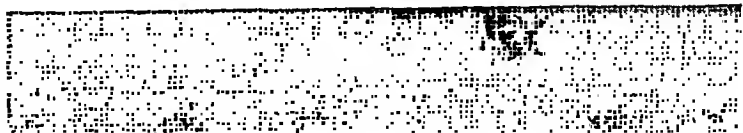
Fig. 1.—Showing three standard leads which were taken shortly after admission and before any medication was given.



Lead 1.



Lead 2.



Lead 3.

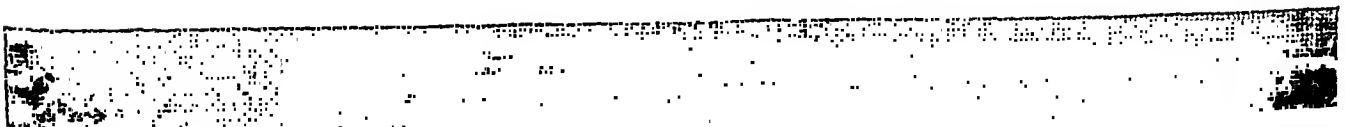


Fig. 2.—Showing the effect of stimulation of the right carotid sinus.

the descriptions are usually vague and incorrect. The literature is full of incorrect reports. Only 172 cases of the real deformity have been traced by Anton, Reitz and Spiegel (1938) and Dannenberg, Anton and Spiegel (1939).

The reverse type of Madelung's deformity is extremely rare. Only five cases have so far been recorded. Our case shows the typical type on the right side and the reverse type on the left side: thus this is the sixth report of such a case.

To be able to diagnose the condition with accuracy, radiological examination is essential. Our case presents all the classical appearances to avoid repetition; these will be enumerated in the case report.

Case report.—The parents of the patient, S. K., Punjabi female, aged 12 years, were told by her drill master that the left hand of the child was not quite normal. This was a year and a half ago. Since then the hand has become deformed progressively into the present state. During the last six months her other hand has been gradually and progressively getting deformed. There is a feeling of weakness and insecurity in the left hand. She feels pain in her wrist if she lifts things with her left hand. There is no history of injury or of abnormal strain. Her past and family history reveal nothing of interest.

She is of normal build for her age, and is slightly anæmic. She is quite intelligent. Secondary sex characters have not yet developed. No evidence of rickets or of hormonal disturbance is present. No other abnormality is discoverable on clinical examination.

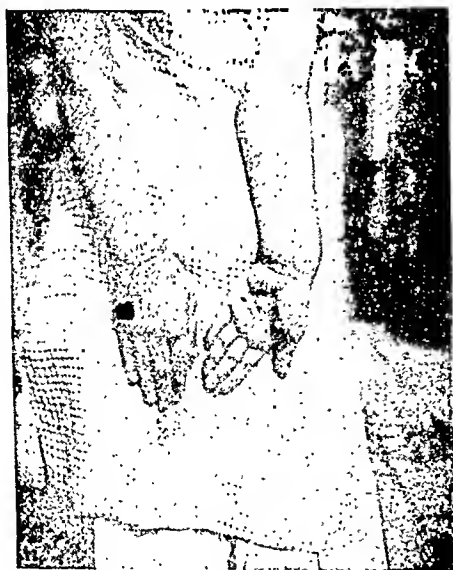


Fig. 1.—Note anterior and lateral curvature of the radius, widening of the interosseous space, anterior dislocation of the lower ulnar head and adduction of the hand on the left side.

The deformity of the hands attracts one's attention, giving the impression of dislocation at the wrist. The radius shows marked anterior

curvature with posterior concavity on the left side. The radius is curved laterally with concavity towards the ulna. The lower end of the ulna is displaced anteriorly and is seen as a small round mass at the anterior surface of the wrist. This hand (the left) is bent medially. The hand is situated on a posterior plane on account of the curvature of the radius. The patient can over-adduct her left hand but cannot abduct it. Flexion is greatly limited; extension is normal at the wrist. The movements of supination and pronation are slightly limited.

The right hand is situated on an anterior plane. The lower end of the ulna is prominent at the posterior surface of the wrist. The movements of adduction, abduction, supination, and pronation of the hand at the wrist joint are normal. The movement of flexion is normal and of extension is limited.

Laboratory examinations

Serum calcium 9.3 mgm.; serum phosphorus (inorganic) 3.8 mgm.; phosphatase 5.8 units (Bodansky). Wassermann reaction is \pm —; total red cell count is 4,460,000 per cmm.; hæmoglobin is 82 per cent of normal; colour index. 0.9; average size is 7.2; leucocyte count is 11,000. per cmm.; neutrophils 52 per cent; lymphocytes 47 per cent (small 43 per cent, large 4 per cent); monocytes 1 per cent; eosinophils, basophils and Türk's cells not present; no abnormal leucocytes were seen.

X-ray appearances (see figures 2 and 3, plate XXII).

1. Lower radial epiphysis. On the right side it is large and irregular and is bent forwards. On the left side, instead of being quadrilateral, the epiphysis is triangular, with the apex of the triangle directed medially. Instead of looking downwards, it is looking downwards and medially, so that the hand is bent medially.

2. The epiphyseal line. On the right side it is losing its distinctness in the medial part. As the medial part of the epiphysis has not yet fully fused, no lateral curvature is seen. On the left side, the epiphyseal line is seen in the lateral part only, and hence the lateral curvature of the radius, on account of the continued growth at the lateral part and stoppage of growth at the medial part. The epiphyseal line has fused anteriorly on the right side, and hence the anterior bending of the radius on this side.

3. The zone of rarefaction. On the right side, decalcification is seen in the epiphyseal and metaphyseal neighbourhood of the medial part of the epiphyseal line. On the left side, this zone of decalcification extends for about $\frac{3}{4}$ inch above the medial part of the epiphyseal line.

4. Osseous excrescences. Tiny projections of bone are seen in the region of the rarefaction on both sides.

5. Lower end of the ulna. On the right side, it is displaced downwards and slightly posteriorly. On the left side, it is displaced

anteriorly. Hyper-condensation of the osseous trabeculae of the lower end of the ulna, as reported by other authors, is not seen in our case.

6. Carpal bones. The deviation of the inferior radial articular surface inwards leads to a diminution of the radio-ulnar articular surface, and the carpal bones get crowded up between the deformed radius and the protruding ulna, taking up a triangular appearance with the semilunar bone at the apex. This is called pyramidalization of carpal bones. Our case shows this pyramidalization on the left side, but not as yet on the right side.

7. Curvature of the radius. The lower end of the right radius is bent anteriorly. Lateral bending is not seen. On the left side, the radius is curved anteriorly and laterally. The lateral curvature leads to widening of the inter-osseous space. This is best seen if the picture is taken in the prone position.

Ætiology

The condition is more common in females ; the ratio of female cases to male cases is 4:1. The condition is essentially an affection of adolescence, occurring in the secondary growth period. It usually begins between the ages of 10 and 14 years. The influence of heredity has been noted in nearly one-third of the reported cases.

There is no history of injury, muscular strain or inflammation. The onset is usually spontaneous without any obvious cause, and the deformity progresses until the complete union of the epiphysis. Deformity of the radius can be caused by injury, rickets, inflammation, tuberculosis and syphilis, but these cases are not cases of Madelung's deformity.

Rickets has been very commonly said to cause this condition ; but as will have been seen, the typical radiological features have not the slightest resemblance to those seen in rickets. Moreover, the blood chemistry and clinical examination in our case do not reveal rickets. Any association with rickets must have been accidental ; most of the reported cases are of the hospital type derived from the poorer classes. The deformity of our case had also been previously diagnosed as being due to rickets, and the patient had received anti-rachitic treatment without any effect.

Since female cases preponderate, an endocrine basis should be considered. Cserey-Pechany gave his two patients glandular ovarian hormone therapy for seven months. He claimed to have checked the course of the disease, and attempted to demonstrate radiological evidence of actual regression of the deformity. It must however be noted that the disease may stop without any medication as spontaneously and insidiously as it began.

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HYPERSENSITIVITY OF THE CAROTID SINUS: REPORT OF A CASE SHOWING SIGNS OF CONGESTIVE HEART FAILURE

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ACCORDING to Best and Taylor (1939), 'carotid sinus' is the term applied to the rather slight enlargement of the common carotid artery at its bifurcation into the internal and external carotids, and it includes a mechanism whereby both pressor and depressor effects are mediated. The afferent fibres of the sinus reflex arc, passing through the sinus nerve, a branch of the glossopharyngeal, make connection centrally with the cardio-inhibitory and vasomotor centres. The efferent fibres of the reflex are in the vagus nerve, although both the vasodilator and constrictor reflexes are abolished by complete removal of the sympathetic chains. Lewis (1932) has shown that attacks of dizziness, fainting and even convulsions may result from overactivity of the sinus reflex, with

(Continued from previous column)

Nature of the condition

The bilateral affection, the premature fusion of the epiphyseal line at isolated sites, the presence of exostosis and the deformed epiphysis give a strong indication that this deformity is due to a dyschondroplasia of the lower radial epiphysis.

Treatment

Osteotomy of the radius after the cessation of growth is the only treatment. Burrows (1937) describes an ingenious operation for the condition.

Summary

1. This is the sixth published report of the reverse type of Madelung's deformity. The typical deformity is seen on the other side. One hundred and seventy-two cases of typical deformity have been described before.

2. The condition is a distinct clinical entity. The criteria of radiological diagnosis are described.

3. The condition should be considered to be a dyschondroplasia of the lower radial epiphysis.

(I have to thank Dr. Khushi Ram Joneja for his help in doing the laboratory examinations for me.)

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marked slowing of the heart and a fall in the arterial blood pressure during the attack. Extra-systoles, delay in A-V conduction, complete heart block or the typical Stokes-Adams syndrome may occur often from no demonstrable cause. Between attacks, slight pressure over the sinus frequently reproduces the symptoms. Weiss *et al.* (1936) believe that the syncope and related manifestations result from one of three mechanisms: (a) cardiac slowing or asystole; (b) primary depression of the blood pressure; or (c) a central reflex to the brain. The last is the rarest type of the three, and it results without either cardiac slowing or a fall in blood pressure; nor, in this last type, is there any diminution in cerebral blood flow. Sigler (1936), in a study of 426 cases which showed cardiac slowing on carotid sinus stimulation, concluded that the condition was more common in males, and that the greatest degree and frequency of slowing occurs in cases with arteriosclerosis and hypertension, the rheumatic heart group coming second, and other general constitutional diseases being third. He felt that the cardio-inhibitory reflex depended upon a vagotonic tendency that is more marked among males, and which becomes still more marked with advancing years. In a still later paper, Sigler (1941) has reported on 1,886 cases showing the hyperactive carotid sinus syndrome, and he has suggested that 'the cardiac inhibition is due to a lowered resistance at the synapses in the cardio-inhibitory centre and more so in the extra-cardiac and intra-cardiac ganglionic cells as well as in the myoneural junctions, allowing the transmission of afferent and efferent impulses in a large and, at times, an overwhelming volume'. He further suggests that coronary disease, with its associated relative ischaemia of the myocardium, is a possible local cause of such lowering of resistance. He therefore believes that a hyperactive carotid sinus reflex may be valuable evidence in the diagnosis of coronary sclerosis, and he also suggests that it might explain various cardiac arrhythmias and even some cases of sudden death. In a still more recent communication, after further study, Sigler (1942) has stated that his findings point to an inherent instability of the vasomotor system, and this instability the test helps to demonstrate. This is particularly true of those cases showing the depression of blood pressure reaction. The seat of this instability is either in the synapses of the medulla or in the vasomotor terminals of the vascular tree, and the arteriosclerosis is possibly one of the underlying predisposing causes of such instability.

Purks (1939) has studied at some length the electrocardiographic changes following carotid sinus stimulation. He studied 67 individuals and found inhibition of the auricle twice, decreased P-wave 12 times, inversion of P-wave once, prolongation of the P-R interval 7 times, bundle-branch block once, and sino-auricular

slowing 49 times. In general, these findings confirmed those of Smith (1937) and Sigler (1934). The most common type of response to both right and left sinus stimulation was sino-auricular slowing. Purks also found, as did Sigler, that there was a great frequency of response in the presence of hypertension and arterial disease, but he suggested that it is much easier to find and compress the carotid sinus of a carotid artery that is hardened by arteriosclerosis or distended by hypertension than it is to find and compress one with poor pulsation.

Although there have been many cases studied showing hypersensitivity of the carotid sinus, nevertheless almost all of them have showed normal sinus rhythm. Weiss and Baker (1933) reported one case with auricular fibrillation, Hiatt and Adams (1940) have reported one with auricular flutter, and Tanney and Lilienfeld (1942) have recently reported four cases, one with normal sinus rhythm, one with paroxysmal tachycardia, one with auricular fibrillation and one with auricular flutter. In these cases of Tanney and Lilienfeld, carotid sinus stimulation produced complete cardiac standstill only in the first case, the other three responding with ventricular asystole only. Their first case also showed pronounced abdominal manifestations which might readily have misdirected the diagnostic effort of the unwary towards the gastro-intestinal tract.

In view of the above, because of certain as yet unreported features shown, and also because of the need of directing our attention once again to the existence of this syndrome, it has been thought worth while to report the following case in some detail:—

J. M., a male Goanese sailor, aged 40, was admitted into the Miraj Medical Centre on 31st August, 1942, complaining of oedema of both legs up to the groins, pain in front of the left ear, dyspnoea and palpitation on exertion, and attacks of vertigo on change of position, especially noticeable when erect. His family history was irrelevant. He had gonorrhoea 12 years previously and had one attack of malaria six years ago. He had no history of rheumatic fever or any cardiac symptoms before the onset of the present complaints. In his habits he was non-vegetarian and he used both tobacco and alcohol moderately. The present complaints were of six months' duration. They were simultaneous in their onset and, since they were persisting, he sought hospitalization. The pain just anterior to the tragus of the left ear, however, had been present for only one week before admission, and it was constant but not severe.

He was well-built physically, weighed 140 lb., placid and usually very co-operative though he feared the results of stimulation of the carotid sinus, and became very tense when he thought the test was likely to be repeated. Abnormal physical findings all pointed towards the cardiovascular system. The cervical veins were not engorged, nor were there abnormal pulsations in the neck. The lungs were clear. The liver was palpable (two fingers) and was slightly tender. There was pitting oedema of both legs to the groins. The cardiac apex was in the 5th space, 1 inch outside the mid-clavicular line. The right border could not be obtained. The precordium was quiet and the cardiac sounds were distant and poorly heard. A loud mitral systolic murmur, unaccompanied by a thrill, was present. Both second sounds were accentuated. The

peripheral arteries were not palpable, and the blood pressure, 180/90 on admission, later ranged from 110 to 140 systolic and 80 to 90 diastolic. The pulse rate was very variable. At times it was only 35 to 40, and then, suddenly, it would exactly double itself for no apparent reason. With the doubling of the heart rate, the murmur would be no longer heard, but it would reappear again when the rate halved itself once more. Compression of the left carotid sinus had no appreciable effect, but compression of the right carotid sinus resulted in stoppage of the heart timed upwards to 30 seconds, with unconsciousness and clonic convulsions, this occurring even when the patient was in the prone position.

Laboratory findings revealed a moderate degree of secondary anaemia and a 2 plus Kahn. Other findings were all normal. An x-ray of the chest showed a somewhat globular heart enlarged both right and left. The electrocardiogram findings are given elsewhere.

The patient was put on bed, rest, potassium iodide, diuretics and bismuth injections, but with no improvement. Atropine, gr. 1/150 q.i.d., was also given, but no improvement occurred until ephedrine hydrochloride, gr. $\frac{1}{2}$ t.i.d., was given. Thereupon the heart rate became steady, ranging from 60 to 80, the oedema cleared and the liver became reduced. While on ephedrine therapy, the attacks of giddiness no longer occurred, and carotid sinus compression would produce cardiac slowing but no asystole or coma. The patient was discharged on 4th November, 1942, and advised to continue the ephedrine hydrochloride. Between 3rd October, 1942 and 8th October, 1942, ephedrine therapy had been discontinued to note the effect. At this time, the pulse rate again fell below 40, and there was recurrence of the vertigo and of the response to carotid sinus stimulation.

Electrocardiogram findings

Figure 1 (plate XXII).—The three standard leads are shown, taken shortly after admission and before any medication was given. The rate is 50.8 per minute and there is both sino-auricular and auriculo-ventricular delay. The depressed S-T intervals and the diphasic T-waves in all three leads indicate myocardial derangement, probably coronary in origin.

Figure 2 (plate XXII).—Here the effect of stimulation of the right carotid sinus is shown. The heart rate before stimulation was 79.0. With stimulation, a complete asystole lasting for 3.24 seconds resulted. This was followed by a heart rate of 31.6 when the heart resumed beating. The heart rate subsequently gradually quickened. The patient was recumbent when the tracing was taken. Lead 2 is shown.

Comment

Our interpretation of this case is that it represents arteriosclerotic heart disease with athero-sclerosis of the coronary arteries and congestive heart failure. In addition, there was S-A and A-V delay in the cardiac impulse, with sinus bradycardia and an undue response to carotid sinus stimulation resulting even at times in what was, to all intents and purposes, a Stokes-Adams syndrome. In keeping with the ideas of Sigler, athero-sclerosis was probably the primary lesion. It is interesting to consider to what extent the cardiac failure was due to the coronary sclerosis and its attendant myocardial damage, and to what extent it was due to the prolonged bradycardia. It should be noted that atropine in the usual therapeutic

doses was ineffective in controlling the condition, whereas ephedrine gave complete relief including a clearing of the signs of congestive failure. This last fact alone would seem to indicate the importance of the rôle played by the cardiac depression in causing the cardiac failure as compared with that of the myocardial damage.

Also the presence of the mitral systolic murmur when the heart rate was slow; and its disappearance when the heart showed a more normal rate, is worthy of note. However, its explanation is obscure.

The sinus bradycardia was undoubtedly due to the hypersensitivity of the carotid sinus causing cardiac depression. The sudden increase in the cardiac rate which would occur from time to time, usually during clinical examination of the patient, may have been due to increased epinephrine production associated with excitement.

The question may well be asked, did the pain just anterior to the left ear represent a glossopharyngeal neuralgia, and, if so, might that not have increased the carotid sinus sensitivity? It has been shown that severing the glossopharyngeal nerve will result in an increased blood pressure lasting several days. This is due to interruption of the afferent fibres of the sinus reflex. Conversely, irritation of the glossopharyngeal nerve would result in increased activity of the cardio-inhibitory centre. This is a possible second explanation of the cardiac depression but it should be noted that it was the right carotid sinus that was overactive and not the left, and also that ear pain had been of comparatively recent origin. This pain, by the way, continued up to the time of discharge.

Summary

1. A case of increased carotid sinus sensitivity in a patient with probable coronary athero-sclerosis is reported.
2. The patient was a special interest because of the presence of sinus bradycardia, S-A and A-V delay and of congestive heart failure.
3. The clinical picture cleared with the administration of ephedrine.
4. It is speculated that the congestive heart failure was due largely to the cardiac inhibition which resulted from the carotid sinus hypersensitivity.

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NORMAL HÆMOGLOBIN VALUES OF THE POPULATION OF BIHAR

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Introduction

DURING recent years, extensive work has been done on anæmia in different provinces of India. The figures for hæmoglobin values of different parts show variations from place to place. The probable reason for such variations appears to be differences in dietary habits and economic status existing among the people. It is possible that well-to-do people of the different provinces do not show such variation, but such persons are few in every province and standards should not be based on them (Napier and Das Gupta, 1935a).

The hæmoglobin content for Bengal and Assam labourers varies between 11.83 and 13.74 gm. per 100 c.cm. of blood. For the middle-class population and students it has been reported as being about 14.50 gm. per 100 c.cm. of blood. Figures for Britain are between 14.50 and 15.60 gm., and for U.S.A. 16.00 gm. per 100 c.cm. of blood. In females the lowest mean figure among the Indian labourer classes has been reported to be 10.40 gm. and the figure for students, Indian as well as European, has been found to be 13.75 gm. Thus, variations among the male population of different places have been noted from 11.83 to 16.00 gm. and among the female population from 10.40 to 13.75 gm. (Napier and Das Gupta, 1941). One standard figure for both the sexes in any locality will not represent a true standard, and so one standard for the male sex and another for the female have to be determined.

An attempt has been made in this work to obtain the hæmoglobin value of two sexes separately. In order to arrive at a truer standard, populations belonging to different social and economic status of both the sexes have been examined.

Methods

The most unfortunate practice of expressing the hæmoglobin in percentage of an arbitrary '100 per cent' normal standard still persists in many provinces of India. This value may mean 13.80 gm. per 100 c.cm. of blood by Haldane's

method or 17.30 gm. per 100 c.cm. by Sahli's method, and thus, when the method employed is not mentioned, a true idea of the hæmoglobin content is not given. Napier and Das Gupta (1941) have rightly remarked that 'hæmoglobin 80 per cent may mean anything between 11.00 and 13.80 gm. of hæmoglobin per 100 c.cm. of blood and this is a discrepancy far from negligible'. An ideal method of hæmoglobin estimation would be actually to determine the amount of oxygen that will combine with a sample of blood, and then estimate the hæmoglobin content. But such a procedure is time-consuming and requires special skill. A very workable accuracy may be achieved if any of the instruments used for the estimation of the hæmoglobin content is calibrated. Napier and Das Gupta (1935a) calibrated a Hellige normal hæmometer by the van Slyke oxygen-carrying method and obtained 13.75 gm. of hæmoglobin representing 100 per cent. In this investigation, a Hellige normal hæmometer has been employed, and 13.75 gm. represents 100 per cent of hæmoglobin.

Technique

The method described by Napier and Das Gupta (1941) has been adopted for the estimation of the hæmoglobin content in this work. Deci-normal hydrochloric acid is placed in the graduated tube up to the 10 mark; blood is taken up in the special pipette to the 20 mark; the point of the pipette is wiped clean so that no blood remains on the outside; the contents are then transferred to the graduated tube containing the acid, and the pipette is washed out with this acid. The tube is allowed to stand for 15 to 20 minutes; it is then placed in the Hellige comparator, and water is added drop by drop until the acid hæmatin solution exactly matches the standard; the height of the lowest point of the meniscus, with the tube held level with the eyes, is then noted, and the reading taken from the percentage figures marked on the tube. After each drop of water was added, the contents of the tube were mixed with the glass rod provided for the purpose, and particular care was taken that as little fluid as possible was allowed to adhere to the rod after each mixing, and that the rod was held in the hand and not placed on blotting paper, so that fluid that does adhere to it will not be lost between each stirring. The hæmoglobin content in grammes per 100 c.cm. of blood was calculated according to Napier and Das Gupta (1935a) from the percentage reading thus obtained from the tube.

Observations

The population was divided into 5 groups according to the social position and economic status of the family; these factors have a definite influence on the quality and quantity of diet consumed. The women have been put in the same five classes according to their family or dietetic status.

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Labourers, poor cultivators and service people earning low wages have been grouped together, because there are no great variations in their diet, which consists of *sattu* (finely crushed parried gram and barley), coarsely crushed maize, *khesari* (*Lathyrus sativa*), potatoes and occasionally green vegetables and milk.

The second group comprises middle-class cultivators, petty craftsmen, small shopkeepers, poor students and poor clerks. Their dietary condition is superior to that of the former group.

Group III consists of people of higher classes, landowners, petty zemindars, clerks, students and businessmen. This group is mainly rice eating, and the diet is deficient in animal products.

Group IV comprises large landowners, zemindars, service people and a few students. Their diet consists of rice and *atta*, milk, vegetable and occasionally of animal products.

Group V consists of zemindars, businessmen, students of well-to-do families and service people drawing about Rs. 200 per month. These people live on a mixed diet, i.e. they regularly consume meat or fish.

There was one odd male on a 'fad' vegetarian diet.

TABLE I

Hæmoglobin value of the population belonging to different economic and social status

Groups	Number on which based	Average hæmoglobin in gm. per 100 c.cm.	Standard deviation
<i>Males</i>			
I	19	10.94	± 0.295
II	21	12.42	± 0.155
III	24	13.63	± 0.073
IV	21	14.12	± 0.0896
V	16	14.70	± 0.159
	1	14.71	..
	102	13.63	..

Weighted average = 13.07

Standard deviation of the mean = ± 0.139

Females

I	21	10.12	± 0.205
II	9	11.42	± 0.219
III	12	13.20	± 0.083
IV	13	14.41	± 0.107
V	16	13.29	± 0.093
	71	12.49	..

Weighted average = 12.04

Standard deviation of the mean = ± 0.137

TABLE II

Hæmoglobin value of population at different ages

Age	Number on which based	Average hæmoglobin in gm. per 100 c.cm.	Standard deviation
<i>Males</i>			
11-20	8	13.54375	± 0.387
21-30	35	13.44700	± 0.262
31-40	31	13.64000	± 0.263
41-50	28	12.92455	± 0.179
	102	13.40	..

Standard deviation of the mean = ± 0.207

Females

11-20	11	12.51600	± 0.286
21-30	32	13.23205	± 0.269
31-40	16	12.30625	± 0.367
41-50	12	12.00325	± 0.219
	71	12.50	..

Standard deviation of the mean = ± 0.296

Discussion

Physiological hæmopoiesis depends on adequate formation of erythrocyte stroma and hæmoglobin, which again are dependent on the supply of anti-pernicious anæmia factor and iron.

Normally iron is obtained from intrinsic and extrinsic sources, the intrinsic source being the conserved iron from the breakdown of the effete erythrocytes, and the extrinsic source being iron contained in daily dietary. Shackleton and McCance (1935) and McCance (1939) have made an exhaustive analysis of the iron content of many foodstuffs. But of more importance than the total iron content is the ionizable nature of the iron which influences its availability for absorption and synthesis into hæmoglobin. The most efficient iron-containing foods are liver, cereals such as dals and oat, dried fruits such as figs and dates, and green vegetables. Red meats, often thought to be rich in iron, have relatively little iron. Widdowson and McCance (1936) show that in certain circumstances a vegetarian diet may be superior to a meat diet for the purposes of available iron. The present investigation shows that vegetarians get their extrinsic supply of iron mostly from cereals such as dals, barley, wheat, rice and green vegetables. For the normal hæmogenesis as far hæmoglobin formation is concerned, 10 to 15 mg. of ionizable iron are required in the daily dietary, and this amount is adequately obtained from cereals consumed by the great majority of the population of this province.

The male population taking a mixed diet or vegetarian diet rich in iron, i.e., the population belonging to the middle class, shows an average hæmoglobin value of 13.914 gm./100 c.cm. of

blood; this figure compares fairly well with the values obtained by different Indian and British workers. Similarly the female population belonging to the middle class shows an average hæmoglobin value of 13.50 gm. per 100 c.cm. of blood. Again this figure approaches very closely that observed by Indian and European workers, i.e. 13.75. The ranges of hæmoglobin values of males and females of different economic and social status of the province are from 9.50 to 15.40 and from 9.10 to 14.98 respectively. The lower class shows a definitely low hæmoglobin value; this is due to the poor nutritional value of the diet consumed by the poor population of the province. So the figures of hæmoglobin values for male and female population for the middle class should be accepted as standard, which are 13.914 gm. and 13.50 gm. per 100 c.cm. of blood respectively.

In the tables arranged on the basis of age, the male population shows no appreciable variation between the ages 11 and 40, but a little lower value has been obtained between the ages 41 and 50. In the female population the highest value has been found between the ages of 21 and 30, while the hæmoglobin values between the ages of 11 and 20 and 31 and 50 are a little lower. Similar results were found by Napier and Das Gupta (1940).

Summary

1. Hæmoglobin has been estimated in 173 persons showing no abnormal signs or symptoms and looking healthy. One hundred and two were males and 71 were females.

2. The standard figure arrived at for the male population is 13.914 gm. and for the female population 13.50 gm. per 100 c.cm. of blood.

3. The population consuming mixed diet or a sufficient quantity of dals and green vegetable, and belonging to different social and economic status has shown very similar average values for hæmoglobin. This has been found true for both the sexes.

4. Males show a higher hæmoglobin value between the ages of 11 and 40 and the females between 21 and 30.

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THE CLAVICULAR SIGN IN CONGENITAL SYPHILIS

By K. D. LAHIRI, M.B., B.S.

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THE enlargement of the sternal end of one or both clavicles in congenital syphilis is known as the 'clavicular sign'.

During the five years I have been working in the Venereal Diseases Department, I have seen it in only 8 per cent of cases of congenital syphilis. The age at which these cases came with the clavicular sign ranged between 8 and 12 years. In all the cases other stigmata of the disease were present; all the patients had a depressed bridge of the nose; the majority had keratitis; the rest had associated syphilitic osteomyelitis and chronic rhinitis. The author (1942) reported four cases of congenital syphilis.

Higoumenakis (1938) has drawn attention to the importance of the enlargement of the clavicle (usually the right) as a diagnostic sign of late congenital syphilis, has reported the presence of this sign in 20 cases of congenital syphilis, and has emphasized that this clavicular sign is superior in its diagnostic value to any other sign of congenital syphilis because of the regularity of its occurrence and the ease with which it may be detected.

Yang (1940) reported 6 cases of late congenital syphilis in which the clavicular sign was present, with considerable enlargement of the medial extremity of the right clavicle, revealed by inspection, palpation and roentgenogram; he has also found bilateral clavicular enlargement in one case.

Nair and Chetty (1942) reported 130 cases of congenital syphilis, and of these 130 cases, 103 cases showed the clavicular sign. They found that the inner third of the clavicle was visibly thick and enlarged, and that the enlargement was unilateral, being on the right side in right-handed persons and on the left side in the left-handed.

Observations

Case 1.—R. C., Hindu male, aged 11 years, did not notice when the swelling over the clavicle started. He came with chronic osteomyelitis of the femur; his blood examination revealed evidence of syphilis and he was referred to the Venereal Diseases Department where a swelling was detected over the right sterno-clavicular junction extending over one-sixth of the clavicle; the swelling was tender on pressure. He was given antisyphilitic treatment with increasing doses of potassium iodide starting from grains 5 thrice daily to grains 15 thrice daily. In about three months the swelling diminished in size, and the pain was not felt on pressure.

Case 2.—Hindu male, aged 12 years, was brought by his father for the treatment of some skin condition, when a swelling was discovered at the sternal end of the right clavicle. It was gathered that he had fever 2 months before, and on the 10th day of his illness he felt pain from the tip of the fingers of the right hand to the right shoulder. The pain was dull and persistent in nature, and was aggravated by movements

Table showing incidence of clavicular sign in congenital syphilis

Case number	Subject	COMMUNITY		Blood W.R.	Clavicular sign	Other stigmata of congenital syphilis	Pain	Result of anti-syphilitic treatment
		Sex	Age					
1	R. C.	H. M.	11	Positive	Unilateral	Osteomyelitis femur and chronic rhinitis.	Present	Partly subsided.
2	D. N.	H. M.	12	"	"	Keratitis	"	Almost disappeared.
3	R. P.	H. M.	9	"	"	"	"	No marked change.
4	P. D.	H. M.	11	"	Bilateral	"	Nil	"
5	M. I.	M. M.	8	"	Unilateral	Osteomyelitis tibia and chronic arthritis.	Present	Partly "subsided."

of the shoulder joint. The painful swelling was about 2 inches in diameter, and was acutely inflamed when the pain first appeared, but there was no pain when he came for examination. The result of the Wassermann test was positive. There was keratitis. He was put on potassium iodide in gradually increasing doses together with other antisyphilitic treatment. He rapidly responded to treatment and the swelling almost subsided, and when he was discharged, slight enlargement of the sternal end of the right clavicle could be detected.

Case 3.—R. P., Hindu male, aged 9 years, a student. Enlargement of the sternal end of the right clavicle was very slight. Slight pain felt on pressure. There were keratitis and Hutchinson's teeth. The Wassermann reaction was positive. Increasing doses of potassium iodide and other antisyphilitic treatment produced no appreciable change in the swelling.

Case 4.—P. D., Hindu male, aged 11 years. Uniform bilateral slight enlargement of the sternal ends of both the clavicles was noticed together with syphilitic keratitis. The Wassermann result was positive. Potassium iodide and other antisyphilitic treatment did not produce any change in the size of the swellings.

Case 5.—M. I., Mohammedan male, aged 8 years, came with osteomyelitis of the right tibia and chronic rhinitis. Wassermann reaction was positive. On examination a small swelling of about $\frac{3}{4}$ inch in diameter was found at the sternal end of the left clavicle. It was tender on pressure. With potassium iodide and other antisyphilitic therapy, the swelling subsided to half its original size.

Discussion

Stokes (1926) found the clavicle thick in 4 per cent of cases and thought that this was not a common sign. Dorne and Zakon (1935) reported 12 cases of clavicular enlargement with a positive Wassermann reaction.

Higoumenakis (1938) showed that the clavicular sign has a diagnostic value equal to other definite signs of congenital syphilis, that it occurs more frequently than other signs of congenital syphilis, and that consequently it is of greater diagnostic value. It is never encountered in persons with acquired syphilis or in healthy persons. According to Higoumenakis, the enlargement of the sternal end of the clavicle as found roentgenologically is due neither to a defect in the statics of the patient nor to a loosening and distension of the articular capsule but merely to an augmentation in the volume of the bone caused by a hyperostosis resulting from syphilitic osteitis. The enlargement usually occurred unilaterally, on the right side in right-handed persons and on the left side in left-handed persons. The explanation of the en-

largement is that the inner third of the clavicle arises from a secondary nucleus which appears between the 18th and 20th year, and the ossification of the bone takes place directly from the connective tissue without the pre-formation of cartilage. The tissue is infected with spirochaetes in the syphilitic child. In early childhood the spirochaetes remain latent locally. The increased activity with the approach of puberty demands increased function of the clavicle. The movement of the arm not only reactivates the spirochaetes but also causes a constant friction of the medial extremity of the clavicle against the sternum, leading to hypertrophy of the sternal end of the clavicle.

Nittis (1937) investigated the sterno-clavicular enlargement in 6 young persons with leprosy at about the age of puberty but the roentgenological result was negative. Yang (1940) observed that at the age of 10 years the second nucleus of the clavicle had not appeared, and the clavicle did not function so actively as during puberty.

Nair and Chetty (1942) found that in certain cases the clavicular enlargement is more confined to the inner end than to the inner third, and in skiagrams found slight prolongation of the inner end upwards and downwards together with the antero-posterior thickening. To the examining finger this gave the impression of broadening with actual enlargement and exostosis of the inner end of the clavicle.

Conclusion

The enlargement of the sternal end of the clavicle in congenital syphilis in children approaching puberty is an important diagnostic sign of congenital syphilis.

Acknowledgment

I am thankful to the Superintendent, Dr. B. P. Varma, and to Dr. H. P. Lal, lecturer in Clinical Surgery, of the Patna Medical College Hospital for permission to publish the case reports.

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ECTOPIC GESTATION

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and

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VICTOR BONNEY says that there is no class of case in which the symptoms supervene with more dramatic suddenness and intensity than in acute tubal rupture, nor any in which prompt and determined surgical measures are rewarded with more pleasurable success. Very true. But here in India, how many cases seek surgical help at once? Very few indeed. From ignorance or fear of hospitalization, and may be because of undue confidence in the barber midwife, the patient more often seeks the latter's help. This crude woman anoints and massages the abdomen so roughly that the whole abdomen becomes tender. Should the patient survive such treatment, the pain becomes so great that she is forced to seek medical aid. To elicit a true history in such a case is often very difficult, and to get her consent to an operation is even more so. There are exceptions, no doubt, but this is the usual kind of case that seeks admission at the King Edward Memorial Hospital, Secunderabad.

It is obvious from what has been said here that in this part of India the diagnosis of ectopic gestation is not always easy. It is easy when you get a patient with a straightforward history, who has not been interfered with. Though it is said that slight abdominal pain associated with much bleeding from the vagina is suggestive of intra-uterine pregnancy, and that much pain with a little bleeding indicates a tubal rupture, the barber midwife, once she handles such a case, destroys these fine aspects of differentiation. Signs and symptoms of internal hæmorrhage, colicky pains, rigidity and tenderness in the lower abdomen, a unilateral pulsatile mass in one of the fornices with marked tenderness in all the fornices, dark red blood on the examining fingers and a history of having missed one or two periods, are very strongly suggestive of tubal rupture or tubal abortion. When there is any doubt, aspiration of dark coloured blood from the pouch of Douglas with an exploratory

needle confirms the diagnosis. The leucocyte count is generally less than 10,000 per c.mm.

The history is often helpful but sometimes it is not. For instance, although it is usual to find a long history of sterility preceding an ectopic gestation, this is not always so. Recently a patient who had had a child 8 months previously was operated on for ruptured ectopic. The absence of a history of amenorrhœa need not exclude a diagnosis of tubal pregnancy; this is demonstrated in two cases in our list of ectopics who denied all such history. On the other hand, positive findings such as soft pulsatile unilateral mass with symptoms of acute onset were caused by an easily-shelled-out pyosalpinx in one case, and a small twisted ovarian cyst in another.

The number of cases submitted to operation in this hospital for ectopic gestation since 1935 is 55; cured 50, died 5, mortality percentage 9.09.

Some interesting cases

Case 1.—A nullipara, aged 31 years. Amenorrhœa for 6 weeks following which the patient had a sudden and severe pain in the lower abdomen, and fainted. There was no bleeding P.V. She was immediately admitted to a hospital, where she was treated for pelvic inflammation for 2 weeks. Finding no relief she put herself in the care of a hakim for 10 weeks. During this period she noticed a swelling in the left side of the abdomen. After the hakim's treatment she started having a red vaginal discharge which had continued for two and a half months prior to admission here.

On admission the patient was very anæmic, and complained of vague pain in the abdomen. Temperature 102°F.; pulse 126 p.m.; R.B.C. $1\frac{1}{2}$ millions per c.mm.; colour index 1. Hæmoglobin value 30 per cent; W.B.C. 15,000 per c.mm. There was a rounded cystic swelling to the left of the middle line, rising up to the umbilicus.

P.V. examination revealed a boggy mass in the left side. The body of the uterus was felt in the right side. X-ray after injecting lipiodol into the cervix showed a dead foetus (18 weeks) in the pelvis, but no lipiodol around the foetus. The patient was put on intensive liver and iron therapy for a few days.

Operation notes.—After a blood transfusion, the abdomen was opened. There was a large extra-uterine gestation sac adherent to the omentum above and the bladder below. The sac was separated and opened. It was completely removed after delivering the foetus and the clots. The peritoneum was drained. The patient made an uneventful recovery.

A possible explanation of the history and findings is as follows:—

A rupture of a tubal pregnancy into the layers of the broad ligament at the 6th week, and a continuation of the pregnancy as a secondary ligamentous pregnancy till the 18th week, followed by the death of the foetus. Evidently bleeding commenced with the death of the foetus, and had continued for the last $2\frac{1}{2}$ months.

Case 2.—A multipara, aged 28 years. Amenorrhœa for 3 months. Slight bleeding for 20 days. Profuse bleeding for 2 days. She was being treated outside as threatened abortion during these 20 days. On admission, her general condition was fair; pulse 136 p.m. A distinct lump in the right iliac fossa. W.B.C. 9,000 per c.mm.

P.V. examination showed the external os patulous and soft. A large tender pulsating mass was found in the pelvis extending into the abdomen on the right

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INIENCEPHALY: A TYPE OF FŒTAL MONSTROSITY

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'FREAKS OF NATURE' are sometimes met with in the realm of obstetrics. One such is 'iniencephaly'. Fœtal monstrosities are of rare occurrence and of them iniencephaly is one of the rarest. A study of this abnormality is interesting. Apart from the anatomist and the embryologist the obstetrician should know something about it. The interest to the obstetrician lies partly in the fact that it can sometimes be diagnosed ante-natally and also that maternal complications arising from it may be prevented.

History

Obstetrical literature reveals the fact that in 1836, Saint Hilaire described 3 cases of a fœtal abnormality, in which the cardinal features were (a) a deficiency of the occiput in the

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side. A brownish red discharge was present. The patient passed a piece of uterine cast during the night.

Operation notes.—A large pelvic hæmatocele on the right side with organizing clots of blood was found. The omentum was adherent to the sac. The sac contained a 12 weeks' fœtus and placental tissue. The cavity was packed with vaseline gauze. Five hundred c.c. of blood were transfused. A stormy convalescence.

Case 3.—The patient complained of a freely movable tumour on the left side of the lower abdomen for 5 months, slightly painful for 10 days. Two children; last child 2 years old. Had amenorrhœa for 5 months during which time she noticed breast changes and nausea. These signs gradually disappeared and she had menstruated regularly for 5 months prior to admission.

P.V. examination.—A tumour the size of a cricket ball freely movable, not tender. Uterus identified separately, normal in size.

Operation notes.—An oval muscular swelling in the middle of the left tube containing a lithopædion of a 5 months' fœtus covered with greyish clots of stale blood; the wall of the tube hypertrophied to 1 inch thickness. A case of intramural rupture of the gestation sac followed by death of the fœtus. Patient discharged cured on the 21st day after operation.

Case 4.—Complained of fever, vomiting and pain in the lower abdomen for 10 days. Pain started in the right iliac fossa and spread. Was massaged and a tampon was used by a *dhai*. No children. Denied all history of amenorrhœa. Menstruation was said to be regular but scanty for the past 4 months, the last period was said to have occurred 15 days before.

Examination.—Tongue dry; temperature 100°F.; pulse 128 p.m.; lower abdomen tense and tender. W.B.C. 9,000 per c.mm.

P.V. cervix soft. A tender boggy mass in the anterior fornix. No discharge.

Operation notes.—Abdominal cavity full of blood. A large pelvic hæmatocele containing a live fœtus of 4 months' size. Placental tissue was found adherent to the anterior fornix, both the iliac fossæ and pelvic colon. Sac was removed as far as possible. Right tube disorganized and was not identified separately. Left tube also removed. Patient made an uneventful recovery.

We are grateful to Colonel John C. Pyper, O.B.E., I.M.S., for helping us to contribute this article.

region of the foramen magnum, (b) spina bifida, and (c) a retroflexion of the spine.

Lewis (1897) classified 22 cases of iniencephaly as—

(a) Iniencephalus clausus (i.e. with no encephalocele),

(b) Iniencephalus apertus (i.e. with encephalocele),

(i) with small encephalocele,

(ii) with encephalocele bigger than cranial contents.

Forty-five cases have been reported up to date. Lately, Howkins and Lawrie (1939) have cited 6 cases. (The facts recorded here under history and ætiology are quoted from Howkins and Lawrie.)

Our cases

Case 1.—Patient, aged 24 years, 6 months' pregnant, was admitted to the hospital with acute pain for 5 days.

Obstetric history.—Two live births and 2 abortions.

Abdominal examination revealed hydramnios, an abdomen tense and tender, fœtal parts palpable, fœtal movements absent, fœtal heart sounds absent.

Measurements normal. P.V. examination revealed cervix 2 fingers dilated and membranes intact.

Anæmia was present, urine was clear; B.P. was 110/70 mm.; Wassermann reaction was later found negative.

Two hours later the membranes were artificially ruptured and delivery occurred 10 hours later. The placenta was retained, and post-partum hæmorrhage followed. Other measures failing, manual removal of the placenta under anæsthesia was done 6 hours after delivery.

Child.—a stillborn male, neck very short, cranium iniencephalus clausus with retroflexion. Limbs, trunks, etc., normal; weight 2 lb. 6 oz.; length 16 inches.

Case 2.—An Anglo-Indian woman, aged 22 years, was examined ante-natally at the Eden out-patient department.

Obstetric history.—Two live births (one Cæsarean and one forceps).

First examination.—Patient 7 months' pregnant.

Abdominal examination showed height of the fundus 4 fingers below the xiphoid process. Head floating, fœtal heart sounds absent, fœtal movements absent.

Blood pressure was 118/75 mm. of Hg.; urine—no albumin; Wassermann reaction negative.

Second examination (after one month).—Height of the fundus—2 fingers below the xiphoid process. Head below, floating, fœtal heart sounds not heard, hydramnios present. Blood pressure 140/80 mm.; urine, albumin present.

On admission.—Uterus contracting and tense, head floating, fœtal heart sounds absent, os one finger tight, membranes intact. Blood pressure 140/80; urine, albumin present.

One-quarter gr. morphia was given and the patient was watched for 2 days. Membranes were then ruptured artificially and the patient was delivered 2 hours later. Severe hæmorrhage necessitated manual removal of the placenta which was adherent to the Cæsarean scar. The puerperium was stormy. Child—a stillborn male; neck, very small; cranium, iniencephalus apertus; limbs, trunks, etc., normal. Weight, 3 lb. 14 oz., length 17 inches. Testes were undescended.

Case 3.—A Hindu woman, aged 26 years, first pregnancy, had no ante-natal examination and was admitted at full term with a slight pain for 3 days, membranes already ruptured. The patient reported absence of any fœtal movement for several days.

The general condition was good; there was no sign of toxæmia. The Wassermann reaction was later reported negative.

Abdominal examination showed a uterus of 36 weeks' size, abdomen tense (hydramnios); the head was not felt at the fundus and pelvic grip was doubtful; foetal movements and heart sounds absent.

Vaginal examination showed the os 2 fingers dilated, the cervix taken up. A rather soft structure was felt presenting, and a breech presentation was diagnosed. The examining finger was stained with a dark reddish discharge.

The patient was watched. Next morning she started bleeding per vaginum and an internal examination was made. Through the full dilated os, the vertex without a vault was felt. The second stage was helped with a cranioclast, and a macerated baby was delivered. Here too manual removal had to be done for retained placenta and hæmorrhage. The puerperium was very stormy. There was high fever, sub-involution and offensive lochia.

Child, stillborn male, no spina bifida, limbs, trunks, etc., normal; weight 7 lb.; length 19 inches.

Case 4.—An Anglo-Indian primipara, aged 18 years, attended the Eden Hospital for antenatal examination.

First examination.—Patient pregnant 8 months, general condition good; no sign of toxæmia, measurements normal, Wassermann negative.

Abdominal examination showed a uterus of 32 to 34 weeks' size, the head floating, and doubtful foetal heart sounds.

Second examination was made on admission about a month later. A full-term pregnancy, slight pain. Membranes were intact.

Abdominal examination showed a tense uterus (hydramnios), head floating and doubtful foetal heart sounds.

The patient was watched. She developed acute hydramnios during her stay in the hospital and was x-rayed. The report was 'the head of foetus not seen? Anencephaly'. The patient stayed for ten days with no sign of onset of labour. She left hospital and was later reported to have been delivered in the Dufferin Hospital of an anencephalic baby.

I am not sure whether this case 4 was definitely a case of iniencephaly since I did not see the foetus, and the radiological evidence was inconclusive.

Analysis of the four cases

All cases came with hydramnios.

All patients were young (18 to 26 years).

There was no sign of toxæmia except in one case.

No hereditary factor could be found.

Two patients were primipara and two multipara.

In the multipara all previous children were healthy.

The third stage of labour was difficult in all cases and manual removal of placenta was needed in all.

The puerperium was associated with rise of temperature in all cases.

No case was diagnosed ante-natally except one in which x-ray was used.

Wassermann reaction was negative in all.

Children—all male; all stillborn; no spina bifida; one had undescended testes.

Ætiology

This is essentially a developmental anomaly. Anatomically, iniencephaly is the result of an arrested and imperfect development of the vertebral column. The central nervous system

develops with the vertebral column and hence the central nervous system is also defective. Howkins and Lawrie state as follows—'At the early stage of the embryo, the paravertebral sclerotome differentiates into two parts: (i) a ventral mass, which forms the vertebral bodies, pedicles and their cranial homologues; (ii) a dorsal mass, which forms the neural arches and vault bones of the cranium. In iniencephaly one or both of these masses are hypoplastic or ill developed'. 'According to Minot (1897) and others, some normal embryos show during the third week an acute lordosis of the spine. This normally springs back and is not seen in the fourth week. The plausible suggestion has been made that in iniencephaly this lordosis persists and closure of the neural arches is thereby mechanically prevented.' Against this, Hawkins cited a case with fairly severe lordosis and with no gross defect in the central nervous system.

Other theorists have suggested that amniotic or intra-uterine pressure or a short cord is primarily responsible. Heredity and syphilis play no part. Foetal anomalies are often attributed to syphilis but this idea is baseless. In all our cases the Wassermann reaction was negative. The influence of an hereditary factor is disproved by the following facts:—

1. The deformity did not occur in the previous or later pregnancies in the same individual; there was no history of similar occurrence in the family.

2. The mothers were normal.

Thus it follows that the cause, whatever it is, is intrinsic in the embryo or foetus. Post-mortem examinations of many of anencephalic monsters have revealed either absence or deficiency of the suprarenals. This has led to the supposition that suprarenal deficiency has some connection with iniencephaly.

Diagnosis

Ante-natal diagnosis is difficult. The presence of hydramnios should indicate the need for a thorough investigation including an x-ray examination.

During labour the presence of hydramnios, a vertex presentation, but the absence of the bony vertex, and antepartum hæmorrhage with no placenta prævia will lead one to suspect anencephaly.

When from abdominal examination a vertex presentation is diagnosed, but on internal examination something soft is felt, the accoucher is apt to diagnose a breech presentation putting more faith on internal examination especially, since abdominal examination is difficult because of excess of liquor amnii.

Alternatively when on internal examination something soft and spongy is felt and the examining finger reveals blood coming from the base of the skull of the anencephalic foetus, placenta prævia is often diagnosed,

Iniencephaly is practically always accompanied by hydramnios. The reason for this is not clear. The hydramnios seems to be of foetal origin.

Management

The guiding principle is that the maternal interest should be the only consideration. Thus if iniencephaly is diagnosed ante-natally, premature labour may be induced by artificial rupture of membranes. During labour nothing energetic need be done. Generally there is no difficulty, the foetus being small.

I wish to thank Professor M. N. Sarkar for his invaluable advice and guidance in compiling this note and Lieut.-Colonel H. E. Murray, I.M.S., the Superintendent, Medical College Hospitals, for granting permission to publish.

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[Note.—This is apparently one variety of the foetal abnormality commonly known as anencephaly. Anencephaly means the absence of the brain, and this name is inaccurately applied to this condition. Iniencephaly (inion—occiput, encephalon—brain) means a condition in which the brain protrudes at the occiput, owing to the absence of the occiput. This name iniencephaly was first given to this deformity by Saint Hilaire and has been subsequently used by accurate writers on the subject including Howkins and Lawrie who in 1939 wrote a paper surveying the literature and recording six cases seen by them in three years.

The condition (as Howkins and Lawrie say) is much more often seen than reported. They could find only about 50 cases in the literature. Dr. Leila Ghosh informs me that in India in large centres of maternity work, such cases crop up occasionally, but rarely do people bother to record these cases. Apparently the idea of the physician is to get rid of the monster as soon as possible and to conceal the matter, and of course parents adopt the same attitude.

Such cases, though rare, are not as rare as is generally believed, but the subject, though interesting, cannot be said to be one of prime importance to the obstetrician. Nevertheless, the editor feels justified in publishing this paper, which however he has rearranged.

In response to an enquiry by the editor, Professor M. Sarkar of the Medical College, Calcutta, writes as follows: 'Anencephaly is the general name given to all cases showing congenital deficiency in the closing of the neural groove and the formation of the cerebral vesicles in the embryo. Iniencephaly is a sub-group of the anencephaly condition in which there is a condition of arrested and imperfect development of the vertebral column. The cases reported by Dr. Poddar had the external appearance of iniencephaly, though we have not definitely found defects in the development of the vertebral column. There was deficiency of the development of the vault of the skull along with the dorsiflexion. Brain vesicles were present.'—EDITOR, *N. M. G.*]

THE POSITION OF PULSES IN A DIET BASED LARGELY ON CEREALS

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and

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For some time, pulses have been engaging attention of the nutrition experts in India, as a very important constituent of the dietary all over the country. This matter was discussed in some detail at the third meeting of the Nutrition Advisory Committee of the Indian Research Fund Association held in New Delhi on 29th November, 1937, and the following recommendation was made: 'Diet surveys have shown that intake of pulses in various parts of the country might be increased with resulting improvement in the nutritive value of diets based largely on cereals'. In this matter, certain questions arise: (1) Are all the common pulses equally good in nutritive value? (2) Could they be tolerated in high proportions in a poor man's diet based mainly on cereals? (3) Does a high pulse diet ultimately produce harmful effects on vital organs such as the kidneys and liver, etc.? (4) Finally, if such a diet leads to damage to these important organs, and hence jeopardizes health and life, is it possible to make it harmless by the addition of some cheap supplements which will help the proper assimilation of the high nitrogen content available from the common Indian pulses and utilize it for maintaining health and promoting growth?

The first question has already been partly dealt with in the light of the available literature on the nutritive value of pulses (Pal, 1939). All these questions form the subject-matter of the present series of investigations.

Experimental

In a previous paper, we (Pal and Singh, 1938) found that 2 oz. (3.5 oz. = 100 g.) of black gram (*Phaseolus mungo*) and 2 oz. of dahl arhar (*Cajanus indicus*) in a diet containing 8 oz. of whole wheat flour (*Triticum vulgare*) and 8 oz. of raw polished rice—that is, a diet containing one part of pulse to four parts of cereal—could not only be well tolerated by rats, but also that its nutritional value is enhanced by the addition of a quarter ounce of sprouted Bengal gram (*Cicer arietinum*). Hence our high pulse diet in the present series of experiments consisted of a higher proportion of pulses, the ratio between pulses and cereals being 1:2. The reasons for selecting such a high proportion of pulses in the diet were: (i) That diet surveys in the neighbourhood of Delhi have shown a very high consumption of pulses as compared to cereals (1:3 or sometimes more) and (ii) that we wished to derive the maximum benefit (if possible) out of the pulses as a cheap integral part of the diet

of the poor Indian, who either cannot afford the luxury of an adequate quantity of animal protein in the diet, or is not in the habit of taking or is debarred from taking it on social and religious grounds.

The experimental diet adopted was as indicated below; the amounts stated were given to 40 rats, this number of rats being equivalent to one man in dietetic requirements.

(i) Parboiled rice (boiled)—containing proteins of high biological value, as well as minerals and vitamin B₁—16 oz.

(ii) Pulse (in a sprouted condition)—containing abundance of protein and vitamins A and C and roughage—8 oz.

(iii) Sodium chloride— $\frac{1}{4}$ oz.

The feeding experiments were conducted in several groups. The first series of experiment was started with 50 young rats, of an average weight of 33 gm., divided into five batches. Each batch received a similar diet, but the nature of the pulse varied. The first batch received lentil (*Lens esculenta*); the second

This feeding experiment was repeated with five batches of young rabbits, each consisting of six animals averaging 691 gm. in weight, but with no better results. In the course of the second and third week, most of the animals belonging to all the groups were dead.

The next series of feeding experiments was started with four groups of young rats consisting of ten each, with an average weight of 33 gm. The first had simply the basal diet consisting of rice and germinated lentils in the ratio of 2 : 1 together with common salt; the second had in addition 3 c.cm. of cod-liver oil; the third had 2 gm. of fresh butter; and the fourth had 2 gm. of yeast. Seven of the first group of animals died between the third and the fifth week, but all the animals belonging to the other three batches were not only living but also appeared to be well and gained in weight. Table I shows the average increase in weight of the second, third and fourth batches of animals, on cod-liver oil, butter and yeast supplements for ten weeks :—

TABLE I

Showing the progress of the four batches of animals for ten weeks

	WEEKS									
	1st	2nd	3rd	4th	5th	6th	7th	8th	9th	10th
1st batch	33.6	38.4	40.8							
2nd batch	35.6	44.2	49.2	55.9	64.4	73.0	73.3	85.6	93.6	93.8
3rd batch	35.5	39.8	45.0	54.1	56.8	59.3	60.0	66.4	66.7	71.7
4th batch	35.4	43.2	46.8	54.2	61.2	61.8	61.1	68.0	72.2	71.8

batch, Bengal gram (*Cicer arietinum*); the third batch, green gram (*Phaseolus radiatus*); the fourth batch, black gram (*Phaseolus mungo*) and the fifth batch, red gram (*Cajanus indicus*). For four weeks animals of all the groups did well, the average weight of the animals at the end of this period being, for the first group 41 gm., for the second 48 gm., for the third 46 gm., for the fourth 45.5 gm. and for the last 53.5 gm. Later animals belonging to all the groups began to die, so that at the end of the eighth week, for which the feeding experiment was planned, there remained only two animals belonging to the first batch, two belonging to the second, four belonging to the third, two belonging to the fourth and four belonging to the fifth group. Post-mortem examination of all the animals dead during the feeding experiment showed congestion and morbid changes in the kidneys and liver which were confirmed by cutting sections and staining them suitably. Even the kidneys and liver of the still surviving animals revealed similar but slighter pathological changes; these facts showed that a high pulse diet in the ratio of 1 : 2 cereals ultimately proved to be damaging to these vital organs.

It is quite evident from table I that whatever harmful effect the high pulse diet had on the animals was removed by the addition of small quantities of cod-liver oil, butter, or yeast, the first proving to be the best of all so far as the gain in weight was concerned.

Histological examination of kidneys and liver of the surviving animals of the first batch, and also of those that died during the course of the feeding experiment, showed intense congestion and hyaline degeneration of the tissues, but the tissues of the animals of all the other three batches were normal and healthy.

Our third series of feeding experiments began with 60 young rats of an average weight of 34 gm., divided into six batches. The first was given the same basal diet as in the previous experiment, whereas the second batch was given 3 c.cm. of coconut oil, the third 100 gm. of carrot, the fourth devitaminized butter (heated to 125° and boiled for 1 hour with passage of oxygen) 2 gm., the fifth autoclaved yeast 2 gm., and the sixth 1 c.cm. of radiostol as supplement. In the course of ten weeks, six of the animals belonging to the first group, five of the second batch, and one each of the third, fourth, fifth and sixth batches died. Table II

shows the weekly progress in weight of the six groups of animals for ten weeks :—

on this inadequate diet was damage done to the liver and kidneys by some toxic product. That

TABLE II

Showing the progress of the six batches of animals for ten weeks

	WEEKS									
	1st	2nd	3rd	4th	5th	6th	7th	8th	9th	10th
1st batch	36.6	44.0	44.5	45.9
2nd batch	39.6	44.2	45.6	48.2	53.9
3rd batch	37.4	44.4	46.6	50.0	53.1	60.1	64.6	67.1	70.4	75.6
4th batch	36.1	39.2	41.9	46.7	52.9	60.5	63.0	66.7	69.0	66.7
5th batch	39.9	44.2	48.0	51.0	52.4	57.2	56.1	61.4	65.6	63.5
6th batch	39.6	49.0	58.4	64.5	69.0	57.8	73.1	79.1	83.9	86.4

Histological examination of the liver and kidney of the surviving animals of the third, fourth, fifth and sixth batches showed a normal and healthy appearance of the gland structure; post-mortem examination of the organs of the dead animals belonging to these batches showed nothing abnormal except congestion. The organs of all the animals, dead or alive, belonging to the first two batches showed extreme grades of distortion and degeneration of the cells of the glomeruli as well as of the medullary portion of the kidneys—and also of the entire hepatic structure. These facts indicated that some toxin had passed to the liver after digestion and absorption of the high pulse diet, and ultimately had passed to the kidney cells through the circulation, damaging these two vital organs. This toxic action appeared to be responsible for the mortality in more than half the animals belonging to these two batches.

The protein and some of the essential amino-acid components of the five common pulses used as constituents of high pulse diets in our first series of feeding experiments were analysed and the following figures obtained :—

a high protein diet causes damage to the kidneys has been reported by Newburgh (1919), Newburgh and Marsh (1925) and Curtis and Newburgh (1927) and also by Polvogt and his co-workers (1923). The last workers observed hyalinization of the glomeruli, hyaline material in the tubules, with adhesions between the glomerulus and capsule in the Malpighian bodies, with infiltration and congestion surrounding the capsules; although other investigators such as Osborne and his associates (1927) and Addis and his co-workers (1926) reported simply hypertrophy of the kidney without internal lesions. According to Hartwell (1928) the success of various workers in feeding with high protein diets suggests that the failure of others with similar diets is due not to a high proportion of protein itself but rather to a deficiency of some other factor, or to a lack of balance between some other constituents. The pathological lesions observed by us in the liver and kidneys of the animals on a high pulse diet were very similar to those described by the first group of investigators, who are of opinion that excessive protein ingestion causes renal injury partic-

TABLE III

Showing percentage of protein and essential amino acids (on a dry basis) in the various pulses used

Name	ESSENTIAL AMINO ACIDS PER CENT ON DRY BASIS			
	Percentage of protein	Cystine	Tyrosine	Tryptophane
Bengal gram (<i>Cicer arietinum</i>)	17.08	0.225	0.236	0.017
Green gram (<i>Phaseolus radiatus</i>)	23.96	0.117	0.128	0.010
Black gram (<i>Phaseolus mungo</i>)	23.92	0.297	0.170	0.009
Lentil (<i>Lens esculenta</i>)	25.06	0.214	0.121	0.031
Red gram (<i>Cajanus indicus</i>)	22.18	0.073	0.049	0.002

Discussion

These different series of experiments prove definitely that a diet containing mainly pulses and cereals in the ratio of 1 : 2 is quite unsuitable for the maintenance of health and life. The cause of death in the case of so many animals

ularly when certain particular proteins are used. The experiments in the hands of Newburgh and his associates show that dried liver, excess of casein, etc., and certain amino-acids such as cystine (Lewis, 1925) when fed in excess or for a prolonged period are nephro-toxic, and they

suggest that the mischief is most probably caused by the amino-acid imbalance. Similar striking evidence of the relationship of amino-acid imbalance to renal and hepatic injury is furnished by the studies of Sullivan, Hess and Sebrrell (1931, 1932) and Lillie (1932). These observations suggest that injuries related to proteins and amino-acids are less severe if the amino-acids are ingested as proteins, or if amino-acids are in certain proportions, but if certain proteins yield certain amino-acids in very large or small amount, they are likely to be injurious if they constitute the principal source of amino-acid in the diet. The present series of experiments in our hands show that pulses, when taken in excess as a source of protein in the diet, most probably fall within this group of unsuitable proteins which prove toxic to the liver and kidneys owing to an imbalance in their amino-acid components. The high cystine and probably tyrosine content of the pulses (table III) is possibly responsible for the amino-acid imbalance leading to hepatic and renal damage.

Thus it appears that in spite of the recommendation of the Nutrition Advisory Committee (1937) that 'intake of pulses in various parts of the country might be increased with resulting improvement in the nutritive value of diets based largely on cereals', the pulses must not be used in excessive quantities in a general dietary. But diet surveys in certain areas in northern India, and animal experiments previously in our hands (Pal and Singh, 1938), show that a high quantity of pulses can be taken not only with impunity but with improvement in health too.

With a view to solving the problem of these contradictory results, a second series of feeding experiments was undertaken after the addition of small quantities of supplements, such as cod-liver oil, butter and yeast to the diet—which showed that all these supplements, even in small quantities, could not only prevent the toxic effects of a high pulse diet, but maintain improvement in health as shown by general appearance and steady increase in weight; cod-liver oil appeared to be the most effective supplement. In these groups of animals the kidney and liver lesions observed in the other groups of animals on the high pulse diet with no supplement as controls were conspicuous by their absence. A similar observation was made by Cox, Smythe and Fishback (1929) who found definite tubular lesions of the nature of acute toxic nephrosis when 0.3, 0.6 and 0.9 per cent of cystine was added to the diet, but when the diet was supplemented by the daily addition of 300 mg. of the Osborne and Wakeman yeast concentrate (B complex), the kidney injury did not occur at all. Similarly Longwell, Hill and Lewis (1932) showed that vitamin B complex in the diet prevents kidney lesions after the administration of much cystine or excess of casein. According to these findings, cystine is not directly nephro-toxic to rats but it is so in the absence of some water-soluble vitamin (B complex).

Hartwell (1928) found that on a synthetic diet containing 20 per cent edestin and 5 gm. yeast extract per 100 gm. dry solid, many young rats die showing typical kidney lesions; these symptoms can be prevented by the addition of more yeast extract to the diet; thus there appeared to be a definite relation between the protein and vitamin B, and it was suggested that different proteins may require various amounts of vitamin B in order that they may be properly metabolized.

In our hands, too, yeast prevented the nephro- and hepato-toxic effects but, curiously, fresh butter and cod-liver oil which are devoid of B complex were equally effective in preventing the nephro-toxic action of the high pulse diet.

Hartwell (1928) further observed that the protective substance was not destroyed by autoclaving at 120° for 4½ to 5 hours, and suggested that it is not thiamin which prevents the renal injury; and since the rabbit synthesizes ascorbic acid, the effect of green food is not attributable to deficiency of this factor. The series of experiments in our hands too showed that there was no lack of thiamin and ascorbic acid in the basal diet (high pulse diet) as the pulse in a sprouted condition contained a sufficient quantity of these factors. So our findings are quite in accordance with Hartwell's regarding the nature of the preventive substance not being either thiamin (B₁) or ascorbic acid.

Boas (1927) postulated the presence of a protective factor X in certain foodstuffs such as dried yeast, milk, raw potato, spinach, cabbage, egg yolk, etc., that possess the power of counter-acting the ill effects resulting from ingestion of dried egg white. This factor is thought to be similar in distribution in many ways to the water-soluble B vitamins but is not identical with either the anti-neuritic or Goldberger's P-P factor. Its resistance to heat and desiccation varies according to the substance in which it is found.

Regarding the nature of the preventive substance, the questions that naturally arise next are: (i) Is it a fat? (ii) Is it vitamin A or carotene? Both fat and vitamin A which are deficient no doubt in the basal high protein diet are present in cod-liver oil and butter as supplements; but they are completely absent from the yeast supplement. It is with a view to investigating the nature of the preventive factor that a second series of feeding experiments was undertaken with coconut oil, autoclaved yeast, devitaminized butter (the temperature raised to 125° and maintained at that temperature in the presence of oxygen to destroy vitamin A completely), carrots and radiostol as supplements. Coconut oil proved quite ineffective as a supplement; thus fat was not responsible for prevention of the nephro- and hepato-toxic effects. Autoclaved yeast, devitaminized butter, carrot and radiostol were more or less effective, as there was only one death recorded in each group; thus it appeared that neither vitamin A nor thiamin

was responsible for this detoxicating effect but something else is present in cod-liver, yeast and butter (thermostable fraction), carrot and radiostol (prepared from yeast) which is capable of rendering a high pulse diet suitable for maintenance of health by preventing its nephro-toxic and hepato-toxic actions.

Diet surveys have also shown a higher intake of *ghee* (clarified butter) and milk along with high pulse diets taken in certain parts of northern India; this may be responsible for preventing the ill effects due to a high pulse content in a diet based on cereals.

So these experiments clearly show that some thermostable accessory food factor which is present in cod-liver oil, butter, yeast, carrot, etc., which is different from other known vitamins, is capable of protecting rats from nephro- and hepato-toxic actions due to a high pulse (protein) diet, and this idea receives further corroboration from Cox and Hudson (1930) who also are of opinion that 'the active substance of the yeast extract which protects rats from cystine nephrosis is probably distinct from any of the known accessory food factors'.

Summary

1. A very high pulse diet based mainly on cereals must not form the diet of the poor people who cannot afford to take a sufficient quantity of *ghee* (clarified butter), fresh butter or milk with it. Small quantities of yeast, cod-liver oil, green vegetables, carrots, and radiostol (B.D.H.) (which is prepared from yeast) may also be used as adequate supplements to prevent damage to the kidneys and liver.

2. A high pulse diet, when taken alone, causes damage to the kidneys and liver, probably by an imbalance due to its amino-acid components. This can be prevented by taking cod-liver oil, butter, yeast, carrot, etc.

3. The preventive substance is a thermostable one and is probably quite distinct from any of the known accessory food factors. The tentative nomenclature of anti-amino-toxic factor is suggested.

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(Concluded at foot of next column)

THE RÔLE OF VITAL LAYER (OR SCHMUTZDECKE) IN SLOW SAND BACTERIOLOGICAL PURIFICATION

By DURGA DAS MITRA, M.Sc., M.B., D.P.H.

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THE upper layer formed on the surface of the slow sand filter does not appear to play the most important part in bacteriological purification. The sand filters at Pulta, with a capacity of about 99 million gallons daily, offer an excellent opportunity to study such actions, as it sometimes becomes necessary to rake a running filter when it tends to choke, which rapidly diminishes the rate of filtration.

Doubts were expressed regarding the efficacy of raking the surface of the filters, in spite of the great amount of investigation done elsewhere, although it is obvious that certain types of water may form mud balls very quickly on the surface of the filter bed, and principally along the walls of the filters, resulting in shrinking of the sand bed from the walls.

The filter rake used consisted of a steel bar about 5 feet in length and carrying 40 or 50 tines about 5 inches long, pointed and fixed at right angles to the supporting bar. Raking consists of pulling the rake the whole length and breadth of the surface of the sand of the filters leaving shallow cuts about $\frac{1}{4}$ inch deep. In many cases raking appeared to prolong the life of the moribund filters, but it has been used only as an emergency measure.

The present discussion is based on 300 random samples of filtrates from raked filters examined during a period of 2½ years (from June 1940 to December 1942) during the different seasons of the year. The samples were examined either the same day or the day following the raking of the filters.

It should be mentioned that raking does not follow scraping but is done to prolong the period between scrapings.

For examination, McConkey's media were used. Five tubes (double strength) were inoculated with 10 c.cm. (each) and 5 tubes (single strength) with 1 c.cm. (each) of every sample. Results were noted at the end of 48 hours' incubation at 37°C.

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TABLE I

Analysis of bacteriological results of 291 samples from raked filters

		COLUMN 1	COLUMN 2	COLUMN 3	COLUMN 4
		Number of samples	+ in 1 c.cm.	+ in 10 c.cm.	- in 10 c.cm.
Examined on the same day	..	31	2	4	25
Examined on the next day	..	260	0	57	203
TOTAL	..	291	2	61	228

Table I shows the results obtained from the investigations on various filters.

Routine weekly examinations were made of the filters before raking. The 2 positive filters under column 2 were positive in 1 c.cm. on the weekly examination but became negative the next day.

Of the 61 filters under column 3, 4 were positive in 1 c.cm. and 20 positive in 10 c.cm. in the weekly examination.

An additional 9 filters were examined and 4 were positive in 1 c.cm. and 3 were positive in 10 c.cm. before raking.

After raking, these 9 filters became negative in 1 c.cm. after a 2 to 4 days' filtration run.

Of the 291 samples in table I, 228 (78 per cent) were negative in 10 c.cm.

An effort was made to secure information regarding the efficiency of the filters at different time-intervals after raking (see table II).

Summary

Three hundred and forty-two samples of filtrates from raked filters were examined.

Generally speaking, raking does not cause deterioration in the bacteriological quality of the filtrate in the great majority of cases, even though the rate of filtration is increased.

Acknowledgments

I desire to express thanks and gratitude to Mr. Sailapati Chatterji, the present Chief Executive Officer, Calcutta Corporation, for encouragement of scientific work, with a view to which he reorganized the Pulta Laboratory in 1939. I am specially indebted and grateful to Mr. B. R. Dyer, the Professor of Sanitary Engineering, All-India Institute of Hygiene and Public Health, for his kind constructive

TABLE II

Time of taking samples		Number of samples	BACTERIOLOGICAL RESULTS		Number of samples in weekly examination + in 10 c.cm.
			- in 10 c.cm.	+ in 10 c.cm.	
Immediately after raking	..	10	10	0	..
1 hour after raking	..	7	4	3	1
2 hours	..	8	8	0	..
3 "	..	11	9	2	2
4 "	..	4	3	1	1
5 "	..	1	1	0	..
6 "	..	1	1	0	..
TOTAL	..	42	36	6	4

These results compared with the results of weekly analysis showed that, several hours after raking, the filters were as efficient as, or more efficient than, they were before.

The raw water after sedimentation in the settling tanks was usually positive in 1 c.cm. or 10 c.cm. It would therefore appear as stated by Parker (1925): 'It seems hard to avoid the deduction that a fair thickness of sand coated with zoogaea is in itself a very efficient filter.'

criticism and elucidation of several points in the paper. Thanks are also due to Dr. M. U. Ahmad, the Health Officer, and Dr. S. K. Ghose, the Analyst, Calcutta Corporation, for encouragement.

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A Mirror of Hospital Practice

THE USE AND ABUSE OF LIQUID PARAFFIN

By L. K. UPAMANYU, M.B., B.S. (Bom.)
(Medical Department, Narsingharh State, C. I.)

Liquid paraffin is not absorbed by the alimentary tract, and is very soothing to the mucous membrane. Hence it is frequently prescribed for chronic constipation. When given with food, it dissolves some of the important fat soluble factors, especially the vitamins which are passed unutilized with the faecal matter. If this goes on for a considerable period, avitaminosis or hypovitaminosis may follow.

I would here like to report three illustrative cases which happened to come under my observation in private practice :—

Case 1.—A Bohra male child, aged 10 months, was brought to me with stomatitis, rhinitis and conjunctivitis of about three months' duration. He had a 'rickety rosary', Harrison's sulcus, enlarged epiphyses and curved shins. When his history was investigated, it was found that he had been given one of the proprietary emulsions of liquid paraffin with hypophosphites for the last eight or nine months. This was immediately stopped, and the patient was put on an emulsified preparation of fish-liver oil re-inforced with calciferol tablets (crushed and added to the emulsion). He was also given local treatment—acriflavine-glycerine paint for the mouth, acriflavine lotion vapour spray for the nose and mercurochrome drops for the eyes. The patient rapidly improved with this treatment.

Case 2.—A Hindu male, aged 32 years, came to me for the treatment of night blindness of six months' duration. After a careful study of the history it was found that he suffered from chronic constipation, and was advised to take liquid paraffin regularly. His constipation was no doubt relieved to some extent but he developed night blindness. He used to have his food in a boarding house. It consisted mainly of polished cereals and pulses, with occasional fruit vegetables and rarely leafy ones. The food was kept on the fire for hours together to keep it hot for all the boarders. He seldom took fruits. He was advised to stop liquid paraffin at once and was prescribed a concentrated solution of vitamin A in a vegetable oil, a preparation of cascara sagrada and aneurin (thiamine chloride) tablets with the result that the original trouble (constipation) and the acquired trouble (night blindness) gradually disappeared.

Case 3.—A Hindu female, aged 23 years, was brought to me for repeated abortions. She had previously given birth to a live child. But as she suffered from chronic constipation she was given liquid paraffin. Her diet consisted mainly of cereals and pulses. Liquid paraffin was stopped. She was given remedies for constipation alone, and she gave birth to a healthy infant in due course.

Conclusion

Liquid paraffin appears to be harmful when taken for a long period, by dissolving the fat soluble food factors and passing them with the faeces. The cases observed were already having a food with a low vitamin content.

[Note.—That prolonged use of liquid paraffin as an aperient prevents the proper absorption of fat soluble vitamins is an important fact, but it is not a new discovery. Reports have been published on this matter in other countries, particularly America, and the

administration of liquid paraffin for long periods is therefore to be avoided, particularly in persons whose diet is already deficient. The shortage of liquid paraffin may thus be a boon.—Editor, I. M. G.]

REPORTING A UNIQUE RESPIRATION RATE OF 119 PER MINUTE AND A PULSE-RESPIRATION RATIO OF 0.96 : 1.0 IN A CASE OF BRONCHO-PNEUMONIA

By RUSTOM J. VAKIL, M.D. (Lond.), M.R.C.P. (Lond.)
(From the King Edward Memorial Hospital, Bombay)

In view of the extreme rarity of certain findings, I take this opportunity of reporting this most unusual case of broncho-pneumonia in a child one year old.

Case report

P. B., a Hindu male child, aged one year and two months, was admitted into the King Edward Memorial Hospital, Bombay, on 27th March, 1943, with a four-days' history of cough, fever and laboured breathing.

On examination, the child was found to be rather under-developed and under-nourished; the nails and conjunctivæ were pale and the lips cyanosed. There was no visible or palpable rigidity of the neck muscles. The eyes, which displayed a vacant stare, were kept open day and night; there was an obvious inability on the part of the child to cry. The temperature on admission was 104°F., the pulse rate was 160, and the respiration rate was 96 per minute.

On percussion, isolated patches of dullness or impaired resonance were detected on both sides of the chest, more so on the right. Rhonchi and medium-pitched crepitations were heard all over the chest, especially at the bases. The condition was diagnosed as broncho-pneumonia of a grave type and the patient was given half a tablet of M.&B. 693, three times a day, in addition to injections of camphor in oil, liver extract and glucose-saline.

On the sixth day of fever, with a temperature of 102°F., the pulse rate was recorded as 164 and the respiration rate as 119 per minute, the latter observation was confirmed by several members of the hospital staff. On the seventh day of fever, the temperature was reported as 103°F., the pulse rate as 104 and the respiration rate as 108 per minute (which gives a pulse: respiration ratio of 0.96 : 1.0).

After the eighth day, there was a steady improvement in the general condition of the patient; the child began once again to cry and to take interest in his surroundings. On the 14th day of fever, when the child was removed from hospital by the mother against medical advice, the temperature was recorded as 101.5°F., the pulse rate as about 120 and the respiration rate as 60 per minute.

Summary

A case is presented, of broncho-pneumonia, in a child aged one, in which a respiration rate of 119 per minute and a 'pulse : respiration ratio' of 0.96 : 1.0 were recorded during the course of the illness.

I am deeply indebted to Dr. A. Hameed, M.D., for permission to publish this case report.

CORRIGENDUM

In the article entitled 'A preliminary note on the preparation of Seitz filter pads in the laboratory' by S. K. Ghose and G. Panja, published in the May number of the *Gazette*, on page 236, left hand column, 16th line from the bottom should read—

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Indian Medical Gazette

SEPTEMBER

THE TOXICITY OF EMETINE

EMETINE is one of the most useful and also one of the most abused drugs in the pharmacopœia. The only real indication for its use is definite clinical evidence, preferably supported by laboratory findings, of infection with *Entamoeba histolytica*. In spite of the fact that it is widely known that even in the tropics much dysentery, and in some areas most dysentery, is not amœbic, one frequently finds emetine being given in dysentery (frequently with no stool examination at all), which on investigation is found to be clinically bacillary, or in vague 'hepatitis' which is quite possibly not caused by amœbic infection. This latter use is sometimes justifiable as a therapeutic test, but the former cannot be too strongly condemned.

One frequently finds emetine being given on the basis of stool examinations made by an inexperienced laboratory worker, and in the absence of definite clinical evidence of amœbic dysentery. The identification of amœbæ and cysts is a matter in which experience and critical judgment are essential. The report of a laboratory worker who does not possess these qualities should always be accepted with caution, particularly in the absence of clinical evidence of amœbic infection.

Emetine is definitely a toxic drug with a cumulative action, and therefore the dose has to be carefully controlled, and also the period of administration. It is hoped that the days of really excessive doses have gone. Napier in his book on *Tropical Medicine* (now in the press) says on this subject:

'Toxic effects of emetine.'—The most disastrous consequences may result from the ill-advised administration of emetine. These results are the more frequent and serious on account of the dramatic early favourable effects on the patients who are being poisoned. During the 1914-18 war, the writer saw many examples of inexperienced medical officers giving two and even three grains of emetine daily for long periods and literally killing their patients, of whose fate they were often quite unaware on account of the frequent evacuations from hospital that are inevitable in war time. In the subsequent years, he has seen athletic young men's hearts disorganized for years through the failure of their medical advisers to realize that they should advocate strict rest in bed during the whole time a patient is taking emetine.

The most dangerous and important effect is on the heart in which it produces myocardial degenerative

changes and alterations in conductivity, with a fall of blood pressure, cardiac irregularity, and acute dilatation as the result of any undue effort. It also may cause acute mental depression, neuritis, myositis, changes in the skin and nails, and diarrhœa, which last-named is likely to be attributed to the dysenteric condition.'

Now the dose of emetine is limited to 1 grain a day.

The days of long-continued administration for several weeks have now, it is hoped, also gone. The course now usually consists of not more than 12 injections, often only 9 or even 6. After 6 daily injections, a 2 or 3 days' break is usually given.

Two questions however remain: Is emetine in the dosage now commonly given and for the limited periods now observed definitely toxic in any considerable proportion of cases? What is the nature of the lesion attributed to the toxic action of emetine?

We will first discuss the first question: Are the limited doses for limited periods toxic? Most of the evidence on this point is based on experimental work on animals. Sollmann states as follows on this matter:

'The effective dosage of emetine seriously overlaps the toxic range (Leake, 1932); indeed toxic phenomena occurred from effective treatment in 80 per cent of the monkeys used (Dobell and Bishop, 1929). Excessive use is followed by accentuation or recurrence of diarrhœa, sometimes by nausea, peripheral palsy, œdema from renal damage, weakness and irregularity of the heart. The dangers are greater in diseased subjects (Pellini and Wallace, 1918).

Toxic and fatal dosage.—Emetine hydrochloride is toxic for most animals, including man, with 10 to 35 mg. per kg., hypodermically (Leake, 1932). Some variability has been reported in commercial samples (R. L. Levy and Rowntree). Clinical fatalities have occurred from about 25 mg. per kg. (*Ibid.*; Leibly, 1930; Dalimier, 1917; Johnson and Murphy, 1917). These accidents do not seem to be connected with variability in the commercial preparations (Lake, 1918) but appear to be explained by cumulative action. Walters and Koch, 1917, find in animals that doses only 1/10 of the minimal single fatal dose became fatal when repeated daily for three weeks.'

Chopra states as follows:

'In adult human subjects the figures for immediate massive toxicity are not known. Fatal results however are to be feared with doses of 0.6 gm. and anything above a dose of 1.2 gm. is probably fatal at once. Eleven doses of 1.9 grains each would probably cause considerable damage in a man weighing 12 stones, while 35 doses of 0.8 grain each would be definitely risky. There should be long intervals (three months) between series of injections or courses to allow the drug to be excreted from the body.

No general disturbances or gastro-intestinal symptoms are produced in man when a therapeutic dose is given by injection.'

The single therapeutic dose of 1 grain is, in a 10 stone man, 1 milligram per kilo. and is well within the limit of safety from toxic effects. All workers however stress the cumulative action of this drug, and there is a unanimity of opinion that the usual therapeutic dose can be continued only for a limited period and that even then some evidence of toxic action will sometimes appear. A special study of this matter was undertaken by Brown who treated 544 cases with emetine hydrochloride and

recorded toxic effects in 23, the most common being a peripheral neuritis. Brown stated that 'distressing complications of emetine therapy are peripheral neuritis and cardiovascular disturbances', although he gave no figures for the incidence of cardiovascular disturbances in his own cases but merely quoted the evidence of others. Brown stated that he had traced 37 reported cases of toxic effects following ordinary therapeutic use of emetine, and that 10 deaths had been reported. He thought that these were only a small fraction of the cases of toxic effects produced by emetine, but he also thought that real cardiac damage was rare.

Thus it may be taken that the ordinary therapeutic course of emetine is accompanied by a certain amount of risk or toxic effects but that the risk is not a very serious one provided that certain precautions are taken. Most authorities recommend that during the period of emetine administration the patient should be kept in bed and that exertion should be reduced to a minimum.

The second question that arises is regarding the nature of the lesion attributed to the toxic action of emetine. Under this point Sollmann states as follows :

'Local and gastro-intestinal effects are relatively mild or absent with hypodermic injections of the ordinary therapeutic doses of emetine hydrochloride. Larger doses produce some nausea, vomiting, depression and pain. Even 0.25 gm. in a single dose caused only persistent nausea (Allan). Cephaeline is more emetic. If emetine solution should accidentally touch the conjunctiva, it is very irritant (Blue, 1915). Bloody diarrhoea in consequence of therapeutic hypodermic emetine injection is probably more common than was formerly supposed; it may be mistaken for recrudescence of the dysentery. Kilgore and Liu (1917) describe several cases of children who received excessive doses under the mistaken notion that they would be more tolerant than adults. The heart muscle shows early functional and histologic damage, cloudy swelling, shrinking and atrophy of the muscle fibres, which may be followed by scarring. The liver and kidneys are affected later, chiefly with congestion and fat infiltration (Chopra, Ghosh and De, 1924; Rinehart and Anderson, 1931).'

Chopra on this subject states as follows :

'The depressing effect of the drug, if given in doses of 1 grain daily for some time, is very marked, the noticeable features occurring after 4th to 6th injections being loss of appetite, nausea, vomiting, abdominal pain and diarrhoea due to gastro-intestinal irritation. Among the serious symptoms of poisoning are an increased pulse rate, listlessness and cardiac depression. There may be general lassitude, disinclination to make an effort, weakness of the legs, tremors of muscles, globus hystericus, cardiac arrhythmia, low blood pressure and a feeling of faintness. General oedema, petechial hæmorrhages, purpuric skin rashes, hæmoptysis and signs of cerebral and pulmonary oedema may also be present. Albuminuria sometimes occurs. Polyneuritis is common and in some cases difficulty in swallowing—a feeling of constriction about the throat and chest—has been noticed. Urticaria and large pruriginous plaques persisting for a month after the last injection have been known to occur even after a few injections. Sudden collapse and death may supervene in some cases. Auscultation of the heart in these cases shows similarity of sounds, and a lack of the muscular element in the first sound.'

Chopra also discusses in detail the neuritis which he says is produced very early after a course of emetine injections and also emetine diarrhoea.

Here again there seems to be considerable unanimity of opinion except in the matter of the heart affection. There is no difference of opinion regarding the fact that emetine administration may cause some disorder of the heart's action, mainly a tachycardia, but some authors have attributed this to actual myocardial damage and others have suggested that it is due mainly more to vagus irritation than to myocardial affection.

In our present number we have an article by Heilig and Visweswar on the cardiac effects of emetine, in which is recorded the almost complete absence of any evidence of myocardial damage in cases given the usual doses for the usual period, the cardiac condition having been studied by cardiograms, orthodiagrams and blood pressure readings. One striking fact about this study is that in 31 out of 45 cases treated and studied, the injections were given by the intravenous route, a procedure which is generally considered to be absolutely contra-indicated; but the authors report that of 15 such cases studied thoroughly by cardiograms, 60 per cent showed evidence of myocardial damage. Another striking fact about the study reported by Heilig and Visweswar is that observations on cardiac action were made after the patient under treatment had undergone severe exertion, another procedure which is considered to be absolutely contra-indicated.

In spite of breaking all the rules, Heilig and Visweswar report the complete absence of any clinical evidence of toxic action of emetine in their 45 cases, the only evidence of damage being obtained in electrocardiographic studies of some of the patients after intravenous injections.

This paper of Heilig and Visweswar is interesting and we have no reason to doubt its accuracy. It is however in marked contrast to the reports of other workers, some of whom report toxic effects and myocardial damage to be relatively common, others having reported them to be rare but definite.

In their paper the authors suggest that the lack of toxic effects may have been due to the absence of cephaeline from the brands of emetine used by them, but it may be taken that all good brands of emetine should be free from cephaeline.

We are quite sure, in fact we have the authors' written statement on this point, that Heilig and Visweswar would not suggest in any way that their work would indicate that care in the administration of emetine is unnecessary. In fact in their article they state that patients undergoing treatment should be kept under constant observation and kept in bed.

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Special Article

ON THE WRITING OF MEDICAL ARTICLES

By JOHN LOWE, M.D.

Introduction.—It has been suggested that an article on the above subject might be useful to the many doctors in India who have or may have material suitable for publication, but who have little experience in writing for publication in English.

Lack of experience may be felt not only by Indians to whom English is a foreign language, but also by doctors whose own language is English. It is quite wrong to think that a doctor whose mother tongue is English will necessarily be able to write a good article in good English. Some poor manuscripts are written by such men, even eminent members of the profession.

Some non-British doctors can write well-produced articles in good English, possibly because, since English is not their mother tongue, they have to give time and thought to the matter. A doctor whose mother tongue is English, or whose general knowledge of English is good (but sometimes not quite so good as he thinks), may have the idea that he, an educated man, can write an article without much thought, and moreover may tend to resent the suggestion that his presentation of his matter and his English are faulty. There are a few fortunate men who can sometimes write a good article in such a way, but they are very few, and to most of us the production of a good article is a laborious process. This labour, however, is amply repaid if the author, when he sees his article in print, can feel that he has said just what he wanted to say in a concise and clear manner, and if the average reader can feel that the article is easy to read, interesting and informative.

After all, the main objects of publication are that the article should be read and that the reader shall profit from the reading. Readers may be patient and painstaking but one should try to make their task as easy as possible. One reads some articles which may contain excellent material, but which are written in such a way that even to read is difficult and to understand

may be impossible. The object of publication is largely defeated.

A colleague recently suggested to the writer that the publication of a learned and difficult article which very few will understand will enhance one's professional reputation. This view is surely shared by few, and we hope that editors will protect us from such writers.

In manuscripts, mistakes in English are much less serious faults than bad presentation and arrangement. Mistakes in English can usually be corrected by an editor with little difficulty. Bad presentation and arrangement are much more serious faults, faults which often cannot be remedied by an editor, and which may therefore cause the article to be rejected.

To most writers, some system in writing is essential to the production of well-arranged and well-written articles. While it is realized that this is largely a personal matter and that other people may have quite different methods, the writer proposes here to try to outline the principles of writing for the medical press which he has adopted as the result of a fairly extensive experience.

The object of writing for publication.—There should be one and only one main object, namely, to record information, experience and ideas which may be useful to other members of the profession. It may seem strange but it is true that writing done mainly with other motives, to advertise the writer, to discredit the ideas of some other person, or to claim priority, always betrays itself, and is often unreadable.

It is true that writing may serve objects other than the main one, and one of the great values of writing is to the writer himself. The careful thinking which writing necessitates, or should necessitate, may be of great value to the writer himself in making him clarify his own ideas. One has often found, when drafting an article or preparing a lecture, that one's own thinking on the subject was confused. If this confusion can be cleared up, then the article or lecture may be of value; but, if not, its value will be very limited and publication is inadvisable. Some articles show evidence of the lack of such clarification. A recent manuscript studied by the present writer contained two completely contradictory statements, which surprised the authors when their attention was drawn to them.

Steps preparatory to writing.—There are two main steps to be taken by an intending writer before beginning to draft the article, the first step being to decide whether there is any adequate reason for writing the article, and the second being to decide what are the main lines of presentation to be adopted.

The first step is best taken by asking oneself two questions: 'Have I any knowledge, experience or ideas on the subject which may be of interest and value to other members of the profession?' 'Have I the necessary data and knowledge of the subject to write on it?' If these two questions were asked and honestly

answered, some articles would never be written. The answer to the first question may be in the affirmative, while the answer to the second question may be 'Not until I have studied the matter and the literature more closely'. This brings up the question of available literature, which in some places in India is certainly a difficult one, but one that can usually be overcome. For writing clinical notes, case reports and other such material, a knowledge of the literature is less important, but for most other articles it is of great importance. An article which ignores or does not do justice to previous work on similar lines is a bad article, however good the rest of the material in it may be. This matter is referred to later.

The second step, the decision on the general lines of the presentation of the material, and the getting together of all the data and material in a form suitable for such a presentation, is a vital one.

The general lines of presentation will depend greatly on the nature of the material and of the journal to which it is to be submitted. Articles on specialized subjects for publication in specialized journals may be highly technical and should give full details; articles for publication in general medical journals such as the *Indian Medical Gazette* should not be so highly technical as to be understandable only to specialists in the subject; technical details should be reduced to the minimum necessary to make the article clear and convincing. Regarding the use of tables some remarks are made later.

Framing the article.—When the main lines of the article and the general method of presentation have been decided, the next step is to draft a framework of the article, consisting of a title and heads and sub-heads for the principal sections and sub-sections. All these heads and sub-heads should be in a logical order, starting from a definite point, working in a definite way up to certain definite conclusions, and usually ending in a summary. These heads and sub-heads may be retained in the final draft or, having served their purpose as a scaffolding, they may be removed. The present writer considers that suitable heads and sub-heads are of great value to the reader in helping him to understand the article as a whole and the relation of one part of the article to another. They are certainly of great value to the writer in various ways, and, above all, in helping him to keep to the point under discussion.

For simpler, shorter articles such as clinical notes, a framework may be very simple and even unnecessary, but for long articles it is usually necessary, and may need to be quite elaborate. The following is a specimen outline of an article recently published in another journal. This outline was drafted (but not by the present author) approximately in this form before one word of the article had been written. Of course, during writing, it may be necessary to modify the framework.

Results of the Mitsuda test in cases of leprosy of different clinical types

- I. Introduction.
- II. Methods of work—
 - (a) Cases tested.
 - (b) Classification of cases.
 - (c) Lepromin used.
 - (d) Reading of results.
- III. Criterion of a positive result.
- IV. Results of the test—
 - (a) In the cases as a whole.
 - (b) In lepromatous cases.
 - (c) In the neural cases.
 - (i) In the 'neuromacular' cases of different varieties.
 - (ii) In the 'simple' neural cases.
 - (iii) In the 'tuberculoid' cases.
 - (iv) In the 'major tuberculoid' cases.
 - (v) In the 'neuro-anæsthetic' cases.
- V. Discussion—
 - (a) Correlation of the results of the lepromin test with bacteriological findings.
 - (b) Correlation of the results of the lepromin test with clinical activity of the 'neuromacular' lesions.
 - (c) Prognostic value of the test—
 - (i) In lepromatous cases.
 - (ii) In neural cases.
 - (iii) In doubtful cases.
- VI. Summary.
- VII. References.

Writing of the first draft.—This should be undertaken only when the data are all ready in a suitable form and when the writer is quite clear what he wants to say and roughly how he wants to say it. This phase resolves itself into the filling in of all the necessary details to the framework already drafted, and the linking together of the different sections of the article. This brings us to the whole question of English composition which is outside the scope of the present notes. Only a few general ideas and suggestions will be presented here.

It cannot be too strongly emphasized that without clear thinking, clear writing is impossible. The root cause of obscurity in writing is very often lack of clarity in the writer's mind.

As far as possible, use simple short common words. If technical terms are to be used, make sure that they are used accurately and spelt correctly. The construction of clauses and sentences should be simple, and sentences should be kept at reasonable length. Every word, every phrase, every sentence should mean something and something definite; all loose and ambiguous expressions should be avoided. Do not hesitate to repeat words or phrases several times if necessary, and even in the same paragraph and sentence, if the word or phrase is good, and conveys just the right shade of meaning;

'elegant variations' are unnecessary and are usually bad English. Punctuate adequately. Avoid the use of clichés, popular phrases often devoid of real meaning. Use metaphors only if you are quite sure that they are accurately used and convey a meaning difficult to convey in any other way; in medical writing they will rarely be needed. Attempts at humour in medical writing are usually to be avoided; few medical writers can succeed in being funny, and an attempt that fails is disastrous.

The use of the third person and not the first person is usually desirable. One occasionally reads an article full of capital 'I's. Such articles rarely read well. Sometimes, however, the use of the first person is necessary, either to the avoidance of a very awkward passive construction, or to the presentation of personal experiences and personal views.

The revision of the first draft.—In the present writer's experience, it is of great value to let a first draft lie untouched for a considerable period, at least a week and preferably longer, before any revision is attempted. One can then return to the subject with a refreshed mind, and one is able at once to detect faults and errors which one has previously missed, and would probably continue to miss if one worked on the manuscript without a break.

It is good practice to undertake the revision according to a definite plan. The first step is to read right through the article from the beginning to the end without a break, checking the general arrangement and presentation, and making sure that the general idea left on the reader's mind is the one which is intended. Such a reading will usually reveal the need for some re-arrangement, which should be made at once. Only when this has been done can the careful reading of the whole manuscript be usefully undertaken.

In this second, detailed reading, one should begin with the title, making sure that it is reasonably brief, accurate, and informative, giving a good indication of the contents of the article. Then every heading, every section and sub-section, every paragraph, every sentence and every word should be read to make sure that it is relevant and that its meaning is clear. One is often surprised to see how much can be cut out without real loss, and sometimes with actual gain.

In revision it often pays to be drastic. Instead of trying to patch up a bad sentence, paragraph, or section, it is often much better to redraft it completely, or else to leave it out.

When the thorough reading and revision of the article, section by section, have been finished, a final reading of the whole article from start to finish is usually needed. One may have overlooked the fact that the revision of one section may necessitate a corresponding modification of another section. It is necessary to make quite sure that each section is not only good in itself, but that it is accurately co-ordinated with other sections.

Even when all this is done, the revision of the article for the press has probably not been completed. Most experienced authors find it very useful to submit their manuscript to the active criticism of colleagues and friends who, coming fresh to the subject, often detect faults missed by the author. Two kinds of criticism are useful; firstly, technical criticism of an experienced professional colleague, and secondly, criticism of language and presentation by a person with a good knowledge of English and of writing, preferably a person whose mother tongue is English. The technical critic must be a technical man, but the literary critic need not be. Sometimes one person can make effectively both types of criticism, but usually two separate readings of the manuscript, one technical and the other literary, are needed. Critics should be asked to find fault with everything they possibly can, and their criticism should be welcomed and met, if necessary, by modifications in manuscript.

At last, but sometimes only after four or five revisions, the article is ready for publication, but the final draft may be very different from the original draft.

Sundry points : Tables.—Regarding the use and abuse of tables much might be said. Tabular matter is of two main kinds. There are text tables which record certain selected facts and findings, and indicate their relation to each other. Such tables, if well done, are very useful. They enable the reader to grasp at a glance certain points which could otherwise be made clear only by a lengthy discussion. Some authors, however, do not realize that, if a table is good, it is usually unnecessary to repeat all the same facts and figures in the text, although of course discussion of tables is often needed. Another point sometimes overlooked is that text tables, to serve their purpose, should be simple, clear and self-explanatory. Sometimes tables are so complicated that they entirely fail to serve the purpose for which they are planned. After drafting a table, one often finds that whole columns can be omitted and other columns simplified.

The other kind of tabular matter is the more or less complete record in tabular form of the observations made in the study which is reported in the article. In some articles, particularly highly technical articles in technical journals, the inclusion of all these facts may be advisable or even necessary. In less technical articles for less technical journals, the publication of the complete data is often unnecessary and, if they are included, they should usually be at the end of the article and not in the text, the article being drafted so as to be understandable without them.

References.—A note on references has already been published in this journal. In submitting an article to any journal, it is advisable to study the system of recording references which is used in that journal (for several different systems are in use), and to prepare references in

accordance with that system. Another point worth mentioning is that references should not be unnecessarily multiplied in order that the article may look more impressive. Reference should be made only to articles that have been studied in the original and have been quoted in the article. If abstracts only have been used, this fact should be mentioned.

Manuscripts.—Manuscripts should if possible be typed, and any typist's errors should be detected and corrected. The typing should be at least double-spaced so as to facilitate the editor's task. Any paragraphs or sections of the article which might be printed in small type (such as clinical notes and collections of details of various kinds, which may illustrate the main line of argument but which are not essential to it) should be indicated in the manuscript. These points, all minor points, help the editor.

The writer and the editor.—A writer should not forget the difficulties of an editor. An editor has to deal with much poor writing. He may have to face the ire of a would-be contributor whose article has been rejected, of an actual contributor whose writing has been heavily edited, or of his readers if matter published is dull, unreadable or confusing. He is probably a well-meaning but rather harassed man. Try not to make his task more difficult. Send him well-planned, well-written, informative material and he will welcome it. At the same time it should be remembered that a good editor is not easily deceived. He can usually tell whether an author really knows what he is writing about. He is not easily deceived by unwarranted claims for originality, either directly made or implied by an author.

Too often an article is written with little or no mention of previous work along similar lines or of similar views expressed by previous workers. An editor usually has access to medical literature; if he finds that important previous work has been ignored or misrepresented he cannot help suspecting that the authors' originality, either claimed or implied, is very doubtful.

[*Note.*—This article was written some time ago, before the author became the editor of this journal. When it was written, the author was a little doubtful whether he would submit it for publication. Now his experience as editor has made him think that publication might serve a useful purpose.

After writing the above article, we read the article by Sir Robert Hutchison which is reprinted on page 452.—EDITOR, *I. M. G.*]

Medical News

TRIUMPHS OF 1942

(From the *Medical Press and Circular*, Vol. 209, 24th March, 1943, p. 179)

THE latest letter tells us that doctors in the United States are now discussing the outstanding advances in

medicine during 1942. First on the list is the development of dicoumarin, which is derived from rotted sweet clover and acts like heparin. Next comes the triumph of the sulphadiazine over its rivals, it now being regarded in the U.S.A. as the most generally acceptable sulphonamide derivative, except in dysentery, when sulphaguanidine is the compound of choice. Then there is the introduction of mecholyl bromide controlling vascular spasm, the renewed study of penicillin and gramicidin as bactericidal agents, and the development of atebine and tolaquina in malaria. Another triumph is the isolation of biotin from the vitamin B complex and the demonstration that brucella cannot grow without it. Other interesting points are the diabetogenic anterior pituitary hormone which destroys the islets of Langerhans, the use of stilboestrol and follutein in the treatment of enlarged or malignant prostate, and the demonstration of a new type of pneumonia, virus pneumonia. All told, twenty-eight items are listed, one of the most unusual being the development of an automatic sewing machine devised by the well-known Singer Company to be used in suturing. Certainly the list is a full one, and very encouraging. The pace at which medical knowledge advances is quickening continuously.

EFFICACY OF TYPHOID INOCULATION : INCIDENCE OF DISEASE DECREASED IN BRITISH ARMY

THERE is still a controversy from time to time over the practice of protective inoculation against typhoid fever, writes *The Times*.

Its opponents claim that better sanitation is accountable for the immense decline in the incidence of the disease since the South African war when it caused more casualties than bullet and shell. Statistical proof has been offered in favour of protective inoculation but has not satisfied everybody.

The recent series of events in the Middle East now seems to vindicate the supporters of inoculation and to reflect great credit upon the Royal Army Medical College staff who have striven to produce efficient inoculation material. The fact is recorded in the *British Medical Journal* to show that Italian prisoners were found to be heavily infected with typhoid fever, developing the disease shortly after capture; epidemic in the British camp was not satisfactorily controlled by injections of the captured Italian inoculation material, but after the use of British 'tab vaccine' the outbreak ceased abruptly.

It was subsequently shown by laboratory tests that the Italian vaccine was not nearly so effective as the R.A.M.C. product.

These tests are suggestive though not conclusive. Experiences of British prisoners in Axis hands in the Middle East are still more convincing. In a large camp, housing thousands of prisoners with primitive sanitation and scanty facilities for washing, dysentery—a disease similarly linked with poor sanitation—broke out at once in a widespread form. There were numerous cases of typhoid fever among Italian troops in the neighbourhood so that an epidemic of this disease in the camp might well have occurred. In fact it did not, much to the surprise of Italian medical officers; and it seems justifiable to conclude that the relative immunity of British troops to typhoid fever was attributable to protective inoculation with the potent vaccine material which they had received.

Good sanitation is important as one form of protection against typhoid fever. But it seems clearly proved that protective inoculation will give an immunity which enables the troops to surmount even dangers of defective sanitation so likely to occur under emergency conditions in the field.

Public Health Section

CHILD WELFARE WORK

THE IMPORTANCE TO THE DOCTOR OF FIRST-HAND KNOWLEDGE OF THE CHILD'S ENVIRONMENT

By MUKTHA SEN, M.B., B.S., D.M.C.W.

(From the All-India Institute of Hygiene and Public Health, Calcutta)

THE aim of the doctor in the child welfare centre, like that of any public health worker, is to help the people to realize the value of, and to practise, methods which will help them to keep healthy and also will improve their health. This is mainly done by health education. Though this education is given in many different ways, the individual approach is regarded as the main method.

For child welfare workers, a unit is a family. Only a visit to the home can give the worker an opportunity to see the whole 'unit' and its environment. That is why home visiting is called the 'back-bone' of the public health programme, especially that of maternity and child welfare. This home visiting is generally done by the health visitors. The doctor in the clinic who has to guide and advise her should know why it is called the 'back-bone'. She should not take the axiom for granted but should personally visit the homes and discover its value.

The need for the doctor to visit the home for proper health work cannot be realized till she begins to see the children both in the homes and at the clinic. Then only she will be able to judge for herself the practicability of the advice given in the centre. Also she will realize the need for knowing the exact condition of the child or its mother at home, and how he or she fits into that environment.

An attempt has been made here to show the importance of this dual work for a public health doctor. A few facts realized during the visits to the homes of the children who attend the welfare centre of the All-India Institute of Hygiene and Public Health, have been mentioned.

1. (a) *Problems of the mother.*—The doctor sees the mother and her child in the centre. But they do not generally form the influential section of the family 'unit'. There is the husband, the bread earner, who is influential but busy, and finds little time to think about the health of the child till the child is perceptibly ill. There is the mother-in-law who is important but wonders why many things which she never did for her children should be done for this child. She also insists on observing old methods generally based on superstition.

The object of educating and advising the mother is to make her independent in the art of keeping good health, to help her to seek and

earn health and not to thrust it on her. The latter is expensive, and results are disappointing and short lived. The co-operation of both mother and family is needed. A co-operative mother, in spite of not getting any encouragement at home, might bring the child to a centre for a few days for extra-nourishment and other help. But this effort cannot last long. On the other hand, if the husband understands and helps her, the response to advice is better. Only a visit to the home can give the doctor the chance to meet the family, discover the viewpoint of the elders, and try to influence them. Most of the husbands and mothers-in-law become more co-operative if the object of the work is explained to them. Many women who are classed as 'non-co-operative' would be put in a different category altogether if their home problems were known.

(b) *Unhealthy social conditions.*—Visits and discussions at the homes reveal the important part that social customs can play in preventing women from seeking medical advice. Some cannot come without a male escort. Some can come only in a rickshaw or a carriage. There are still others who cannot get out of the house, because of strict purdah. A woman, the mother of four children and married for 12 years, said that since her marriage she had not gone down the steps of her house.

It is really the poor and lower middle class who seem to be more tied down by these customs and to suffer their disadvantages. Preventive measures have to be introduced in this class with more vigour, as they generally neither seek nor can afford proper curative help. Home visiting will give the doctor the opportunity to meet these women who need her advice and help. Such social conditions can be cured only by educating the men, which can be done to a certain extent during home visits, which therefore should form a part of proper child welfare work.

(c) *Difficulties in keeping clean.*—Mothers and children often come to the centre dirtily dressed. Want of enough clothing for changes, want of a place to wash, scarcity of water and lack of money for soap, each contributes its share to this unclean appearance of the mother. Also she lives always in the midst of dirt and dust, and the special longing for cleanliness cannot come till she realizes the comfort and the joy of being clean.

In the bustee served by the Institute Welfare Centre, there is a structure with 18 rooms. Each room is about 5 feet by 8 feet, and shelters one family. For all these rooms there is one bathing place with a single tap. During the few hours when water is distributed in the city, each woman has to do all the work that needs water at

this tap, and store the water for the day. One can imagine how much time can be spent by each woman at the tap. By actually seeing her in the midst of these difficulties one can understand her indifference to the cleanliness of herself and her children.

(d) *Difficulty in teaching clean habits.*—Clean habits are completely lacking in some children. The environment in which they live explains this to a certain extent and the indifference of the mother. To cite one example; in the bustee above-mentioned, there were two small latrines for about 40 human beings. It is difficult to get one empty just when the children need it, so they defecate anywhere. The child has no chance to develop clean habits, and copies the dirty habits of other children.

(e) *Want of time.*—What is wanted is that the mothers should bring their healthy babies at regular intervals to the centre, for weighing advice. Often they cannot spare so much time and so fail to come. That want of time is a fairly strong reason even in middle-class homes becomes apparent when the home is visited. Most of them have only a part-time servant for washing purposes. If she is not in the house when the servant comes, she cannot get him till the next day. The mother has also to cook and send her husband in time to office and children to school. One feels that only a certain preventive sense could make her spend two to three hours in the clinic, just to assure herself about the good health of the baby when she thinks the child is well. Yet there is quite a good attendance of 'well' children at the clinic (71.7 per cent of the total visits).

2. *Social contact with mother.*—Generally a visit to the doctor, or a visit by the doctor to the house, is associated with some unhappiness and sickness. But if the doctor does some home visiting in normal times, the mother sees the doctor at home as one of her own kind, a friend and a sympathizer who has come of her own accord to know her (the mother's) problems, and help her in solving them. The mother has a changed feeling when the doctor sits beside her on the mat, squats near the little cot of her baby, peeps into the food she is cooking and asks her some homely questions in her natural surroundings.

In this stage of preventive medicine in India, when it is viewed with suspicion by a large proportion of the illiterate public, this kind of contact which induces understanding and confidence in the mother and her family is most essential for their co-operation.

3. *Essential needs of the child.*—A home visit often helps us to see the wants of a child not as he is comfortably sitting on his mother's lap when he is brought to be shown to the doctor in the clinic, but as one who might be very uncomfortable and unhappy in his house where he spends 24 hours of the day. Two adults, one toddler and two infants (twins) have been found living in one room 4½ feet by 6 feet with

practically no ventilation, in a pucca building. The single door opened on a narrow pathway with a high wall opposite to it. Very little fresh air and no sunlight could enter the house. There was a badly-kept latrine next door. A lamp was necessary in order to see the inside of the house at 9-30 a.m. The children were subject to frequent attacks of bronchitis.

A doctor who sees such children only in the clinic might be satisfied with giving them medicine or extra nourishment. What they really need is some fresh air and sunlight, before anything else can have any good effect on the health of the children.

4. *Friendship with the toddler.*—The children, especially the toddler, cannot cultivate friendship with the doctor if he sees her only in the clinic. There he sees her with a strange thing (stethoscope) round her neck. Also he associates her with the unpleasant experiences he has: being stripped to take the weight or measurement, or being pricked for a drop of blood, or being made to open his mouth to see his throat, or as one who gives him medicine. But if he sees her in his own house and finds that she can behave in the same way as his mother does, he does not get frightened of her and behaves more freely and becomes her friend. This makes the thorough examination of the toddler easier.

5. *Supervision of the 'field worker' and understanding of her problems.*—Another essential gain for the doctor is that home visits act as a sort of supervision, and also brings more co-operation and co-ordination between the field worker such as the health visitor and the doctor. Often the health visitor's work is judged by her ability to bring the mothers to the centre. There is no doubt that this is an acid test of her work. But here two parties are concerned. One is the worker (who, some mothers think, comes to do her work in order to earn her bread) and the other is the mother. Only by home visiting can a doctor realize that the result of the health visitor's work may appear to be poor, even if she knows what to teach and how to teach, and does her work well, because of the lack of response from the mothers. Many other difficulties that face her, e.g., that of transport (not such a problem in the city), the ignorance of the people, the poverty that limits her advice, etc., can be appreciated by the doctor only by visiting the homes. Sometimes people can be very rude and this may dishearten a beginner very much. Though it is 8 years since the Institute Centre was started, and most of the people in the area are aware of its object and existence, it is not very rare even now to meet with rude treatment.

A mother was advised to have her child of 3 weeks vaccinated by our health visitor, as there was a case of small-pox in the house, which consisted of one room in a bustee. A vaccinator seems to have gone and dissuaded them from vaccinating at that young age. When we went

to see the child at the age of one month, the grandmother would not give us a chance to see the child, but scolded us for giving wrong advice, for she said, even a vaccinator knows better. She wished that people who give wrong advice and thus may cause the death of children should not approach her house. This is an example not only of the ignorance of the people, but also of the want of co-operation and understanding between organizations whose object is public health. A good health visitor's work may be ineffective for such reasons. On the other hand, a bad health visitor's work may be easily detected and controlled.

6. *Better contact with the medical and social workers in the area.*—The private practitioners of the area are generally either indifferent to us or in some cases view us with suspicion. The latter is due to the idea that we encroach upon their private practice. Personal touch with them and better explanation of the public health mode of work, will be made possible by home visits. It will not be difficult to convince them that our work, instead of hindering the work of the private practitioner, will only help it, as healthy babies are our greatest concern and when disease is detected they are referred to private practitioners or hospitals. It is obvious to any public health worker what co-operation from private practitioners means.

At times good advice is contradicted by the family doctor. It often happens that when breast-feeding is advised in cases of diarrhoea in children, he tells them to feed the child on barley water and not breast milk. At the centre, solids are advocated for children from the age of 6 months, but he tells the mother that it is bad for the liver. A contact with the family doctor helps us to know his viewpoint and clear up doubts.

Contact with the social organizations in the area is of immense value for the smooth and correct working of any welfare scheme. Home visits should facilitate this contact.

7. *Knowledge of diet.*—At the house the kind of food the mother and child take, and the way of cooking can be seen. This will help when we want to improve her diet. We can advise, within the means of her purse, a food which is more nutritious and also acceptable.

8. *Better clinic attendance.*—To know the doctor personally will act as a stimulus to some women who otherwise would not come to the clinic, especially as the work of the health visitor is not yet very well known in India to lay people. Some women who had lived in our area and had never come to the clinic before, came after the doctor's visit to the home.

9. *Nomenclature of 'health visitor' in the vernacular.*—In European countries they all know what is meant by a 'health visitor'. We have no corresponding name in any vernacular. So the people call her 'nurse'. This name is always associated with disease and hospital. So often the health teaching the health visitor

does is not considered as her main work by the people. The effectiveness of her teaching consequently suffers, as becomes apparent during the home visits. This meaning given to the name 'health visitor' may be partly responsible for our difficulty in making the people distinguish between a hospital and a clinic. To give a different picture of our work and object, a simple, understandable nomenclature for the health visitor is urgently needed.

10. *A general picture of the community.*—Home visiting gives a broad idea of the general outlook of the community as a whole, the social customs, economic status, the sanitary condition of the area and the problems of the people. We all know that habit forms a great part of one's life. So in order to know the women's interest and their lines of thought, and on this knowledge to build our method of approach and advice, it is essential to have a background of their environment. It will be easier for them and gratifying to us if we can imperceptibly lead them slowly to change their mode of living to a more healthful one. A complete picture of the community will help in planning the programme of work in the right way.

Current Topics

The Decay of Medical Language

(From the *New Zealand Medical Journal*, Vol. 41, December 1942, p. 235)

THERE has been comment recently on the choice of name for important medical posts in New Zealand; particularly those of 'Neuro-surgeon' to the Dunedin Hospital and 'Nutritionist' in the Department of Health. Such words—and many others in common medical use—lack style, are devoid of grace and detract from the status of whoever or whatever they describe. It is no explanation that this is an accepted terminology in the United States; what is fitting in an American background is not necessarily suitable to our own language traditions. As Sir Arthur Quiller-Couch has it, men of science are making discoveries at a rate which leaves their skill in words outstripped and they would bombast out our dictionaries with monstrously invented words that not only would have made Quintilian stare and gasp, but would affront the decently literate of any age.

Over many years there has been progressive decay in the language of our profession. This is shown in different ways and many factors produce it. Some of these undesirable elements deserve detailed comment because they are easily remedied. Medical idiom has deteriorated as part of a general decay in the English language in which the professional side shares. Lord Dunsany, an authoritative writer on this subject, attributes much of the decline to ignorance of the proper use of adjectives. To obtain vivid effect in writing, particularly in the press, nouns frequently displace adjectives; thus 'a strange man in an expensive car' becomes 'a mystery man in a luxury car'. The general effect of such a technique is to produce a disuse atrophy of many useful and descriptive words. In medical writing this is reflected in poverty of expression and lack of skill in clinical description. A few adjectival stalwarts are grossly overworked. This tendency led a distinguished medical writer so long as twenty-five years ago to advocate the formation of a Society

for the Prevention of Cruelty to Adjectives. A good example of the overworked medical adjective is 'marked', which is used to express so many qualities as to have become almost meaningless. It replaces great, copious, abundant, large, tangible, evident, perceptible, clear, unmistakable, decided, pronounced and others. In many cases its effect is purely emotional and has the same significance as the word 'bloody' in other fraternities. The word 'definite' has come to have a special meaning in our hands, the reverse of its content in general use. When a doctor says 'there was enlargement of the spleen' we cannot misunderstand him; when he says 'there was definite enlargement of the spleen' he introduces an element of doubt, almost as if he was surprised at the finding and perhaps not quite sure of it. In any case he has added nothing to his description and if he uses the phrase to three of his colleagues, one will believe that the spleen was considerably enlarged, another that the enlargement was slight, while the third, with perhaps greater insight, will assume the size of the organ to be within normal limits. The essence of professional description is to convey the same meaning to all who read or listen; if this be so then the word 'definite' and its objectionable partner 'very' might well be omitted from medical idiom.

There is not sufficient distinction in the medical mind between the spoken and the written word. Certain medical slang is highly descriptive and emotionally and intellectually suited to the purpose of professional discussion; when, however, such idiom is transferred to print it produces a different effect. There are too many examples of words and phrases incorporated and accepted into the medical press which offend against rules of style and grammar. Textbooks on 'the acute abdomen' are numerous: disease may be acute, but an abdomen, never. Exactness and dignity are the two essential qualities of good medical expression. The surgeon who 'laparotomizes' his patient and the physician who diagnoses 'P.T.B.' achieve neither.

If anyone doubts that our clinical language has declined let him compare the average medical journal of to-day with the published writings of Bright (1827) or Addison (1855). The medical author of last century wielded a mighty pen; his literary style was arresting, his descriptive talent considerable and he used with skill a vocabulary far more extensive than the average to-day. The strength of medical writing in Victorian England lay in the classical education with its insistence on literary expression, which was common to all schools of the time. The old educational order, once summed up as 'classics in the morning, mathematics in the afternoon', has given place to education based on vocational considerations. This may be well, but it is salutary to remember that the professional men of to-day who show special skill with the pen or who express themselves more ably than their colleagues are largely drawn from the ranks of those who were given this classical education. They sat at the feet of masters who believed the Greek language to be the one essential educational instrument. Frank Fletcher, late headmaster of Charterhouse, who has played a leading part in English public school education for many years, draws attention to the dangers of the present tendency to specialize in education at an early age. So far as the medical profession is concerned he has this to say:

A boy who wishes to be a doctor may have a real gift and taste for language and scholarship: but he cannot afford to follow a classical or literary course. The demands of the science examinations required for a medical degree, preparation for which is being forced more and more back on the schools by the universities,* are too urgent to allow him to develop freely along the line which we should otherwise choose for him. What the medical profession has gained in scientific knowledge by these demands is balanced by a loss in

general culture that may in the long run react upon their scientific and professional efficiency. There have been complaints from older men in the hospitals and at the universities that their medical and scientific pupils now are less receptive of their lectures and teaching than the former products of a more literary or at any rate less specialized curriculum.

Fletcher might have added that lack of scholarship is a disability not only to the student but to the graduate, who finds himself unable to hold the interest and attention of his colleagues in debate and expresses himself on paper without eagerness or distinction. These intellectual defects in the profession, which are now so universal that they escape comment, have a much wider and more serious significance than in their application to professional language. This was expressed by Professor John A. Ryle in an article entitled 'The Future of Medical Education as seen by a Teacher', in the *British Medical Journal* of 6th September, 1941.

If there is one thing which medicine has shown a tendency to sacrifice in return for the rapid contributions of the sciences to its instruction and practice, it is perhaps its position as a cultural profession. Its philosophy has not kept pace with technical achievement.

It is customary to describe one whose powers of expression are above the average as having a good 'choice of words'. This goes to the heart of the matter. Choice means careful selection and requires thought. The doctor who expresses himself with clarity and precision thinks before he speaks. He has established a lifelong habit which gives him speed in choosing the right word for any shade of meaning. Many have not acquired this habit and rely on the stereotyped solecisms of a strictly limited medical jargon, which come so easily to the tongue. Too often these unworthy phrases find their way into print. No doubt the pendulum will swing again and the profession demand a higher standard of literary expression than at present prevails. Meanwhile it is not too late to hope that he will shortly welcome a neurological surgeon, whose unit will receive support from all parts of the Dominion.

Medical Literature*

By SIR ROBERT HUTCHISON, Bt.,
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(From the *Lancet*, 18th November, 1939, p. 1059)

It will be agreed, I think, that the amount of the writings of a profession is a measure of its vitality and activity, whilst their quality is a rough indication of its intellectual state. Medical literature; to take our own case, is the currency or medium of exchange by which a man contributes to or borrows from the common stock of knowledge and experience, and the volume of this currency and the character of its metal are of the greatest importance to us all.

ITS BULK

Surveying contemporary medical literature, the first thing that impresses one is its bulk. Go into any large medical library and see the hundreds of periodicals spread out on its tables and the thousands of books on the shelves which line its walls and you cannot fail to be struck—perhaps appalled—by it. Professor Bulloch, who has given great attention to this subject, estimates† that there are over 5,000 medical periodicals of one sort or another in the world; others have put the number as high as 7,000. In this country alone, and we are more modest in our output than many of our neighbours, there are about 130. The number of medical books is of course much greater, the yearly crop of them in Great Britain amounting to more than 400; what it may be for the whole world I am unable

* We believe that in England it is now planned to alter this, to encourage a good general if not classical education and to leave 'premedical' subjects to be taught in medical school.—EDITOR.

*The Lloyd Roberts lecture delivered before the Medical Society of London on 16th November.
†Schorstein lecture. *Brit. Med. J.*, 1935, 2, 810.

to say. The matter can be put in another way: there have been, to quote Professor Bulloch again, on an average two articles published on tuberculosis alone every day for the last 40 years. This gives one some idea of the immense fecundity of the medical press. There is no need, however, to labour the point; to paraphrase the words of a famous resolution, medical literature 'has increased, is increasing and ought to be diminished'. For let there be no mistake about it, this enormous proliferation, this pullulating and fungus-like growth is both a nuisance and a danger. The mere question of storage is itself a problem. In the library of the Royal Society of Medicine room has to be found for 3,000 additional volumes each year, and these take up 60 feet of shelving 8 feet high. In a private house it is now impossible to find room even for bound volumes of the weekly journals, while in the modern flat the only room big enough to hold anything larger than a duodecimo is the bathroom. The consequence is that tons of medical journals must be thrown into the dustbins every week.

This, however, is merely the mechanical aspect of the question; more serious is the effect on the very purpose for which medical literature exists—the record and interchange of knowledge. As every delver in the mass knows, it is becoming increasingly difficult to find the needle in the haystack, the few grains in the heap of chaff. Facts may be said to be buried rather than recorded and the fruits of the labours of our predecessors are apt to be lost. More and more, too, is it difficult for the workers in one field to keep in touch with what is being done in others.

Bacon, in one of the aphorisms in the 'Novum Organum', says that 'when a man addresses himself to discover something he first seeks out and sees before him all that has been said about it by others', but it is almost physically impossible for anyone to do that now, and young writers seem often to ignore almost entirely the previous work on their subject. I am aware that this practice has been defended on the ground that reading up what other people have done tends to make the mind lose its freedom. There may be some truth in this, but none the less, neglect of the previous literature must necessarily involve much needless repetition of effort and searching for that which has already been found, besides making it difficult for the investigator to see his subject in correct focus. The case of those, and they are the great majority of us, who are not investigators but who read only to learn and to keep abreast of current knowledge, is equally hard. Snowed-under by an increasing avalanche of publications, their attention becomes wearied and dissipated till they are tempted to give up in despair.

HOW TO COPE WITH IT

What, then, is to be done? Must we sit still and see science suffocated in its own secretions or can we do anything to mitigate the evil? If that is impossible, how can we as individuals make the best use of medical literature without being overwhelmed by it?

There are some, to consider the last question first, who get over the difficulty by simply ignoring medical publications altogether. I remember, for instance, going into the room of a practitioner, a man of much general reading, and seeing on the floor a large heap of weekly medical journals still enclosed in their wrappers. On my asking him why he kept them there if he did not mean to read them, he replied that he found them useful to throw at the cat! I have also been told, although the story may be apocryphal, of a young doctor who went down to act as holiday locum for a practitioner in the country. The practitioner before leaving told the young man that he would have the run of the whole house except for one room which he must not enter. Needless to say, no sooner had the holiday-maker gone off than the young man made his way into this Bluebeard's chamber only to find it stuffed from floor to ceiling with unopened medical journals. Such was the elderly practitioner's grisly secret. Many of us, it must be

confessed, though not so negligent as he, at least welcome the relief of receiving in August or September the students numbers which contain nothing requiring attention and which therefore afford us a temporary respite. For current medical literature cannot be permanently ignored with impunity. As Osler said, 'A doctor who does not use books and journals, who does not need a library, who does not read one or more of the best weeklies and monthlies, soon sinks to the level of the cross-counter prescriber, and not alone in practice, but in those mercenary feelings and habits which characterize a trade.'

All the busy practitioner can do is to tear out from his weekly journal those articles which interest him and which have a direct bearing on his work, and file them. In this way he will build up a collection to which, if it is properly indexed, he can refer as need arises. If, in addition, he gets every year such a publication as the *Medical Annual*, it should not be difficult for him to keep reasonably up to date.

For the contributor to medical literature, however, who takes into account the work of others this is not enough. He needs in the first place a clue through the labyrinth—a directory to help him to find the publications relevant to his own work—and fortunately we have in the *Quarterly Cumulative Index* an excellent guide of this sort to the producers of which medical writers can never be sufficiently grateful.*

The next difficulty may be to find the particular journal in which the required paper has appeared. There was an interesting discussion on this point last summer in the correspondence columns of *The Lancet*,† originated by Professor McDowall, in which several contributors laid emphasis on the importance of greater co-operation amongst different libraries so that their resources in the form of the less known journals could be pooled for the benefit of readers. No doubt much might be done on these lines to make it easier to consult the rarer publications.

'GETTING UP THE LITERATURE'

But when the required articles have been found they have still to be read and abstracted. This is a laborious business which requires also nowadays a considerable knowledge of foreign languages, and more and more there is a tendency, which seems to have originated in America, to have bibliographies prepared and abstracts made by professional librarians. I confess I view this labour-saving device with no great favour. It seems best for each writer to do his own quarrying, for the librarian, however skilled in his own business, has had no medical training and cannot be expected to know the relative value of different papers nor the points in any which should be picked out. He has therefore perforce to confine himself to a transcription of the summary of the paper, if a summary is given, but for the conscientious original writer such a summary is not enough. The only excuse, indeed, for this way of 'getting up the literature' is when the paper is written in some outlandish language, with which a librarian may have at least a working acquaintance, or when the student lives remote from any large medical library. In such a case, however, it is now possible to send a photostat copy of any article required and that is far better than a mere abstract made by someone else.

The work of the literature-hunter would be easier were there more periodical publications of abstracts like the German *Zentralblätter* and *Jahresberichte*. The Medical Research Council produced such a publication for a few years (*Medical Science: Abstracts and Reviews*) which was of great value, but unfortunately it came to an end, and in my own sphere of work I have found *Nutrition Abstracts* very helpful, but even some volumes of abstracts have come to

* Mr. Leslie Morton's book 'How to use a Medical Library' (London: John Bale) may be studied with advantage by all readers.

† *Lancet*, 1939, 1, 1401, et seq.

reach a portentous bulk. The ideal, of course, would be an international clearing-house in which the whole periodical medical literature of the world would be sifted by experts and summaries made of such papers as contained any original as opposed to merely repetitive or didactic matter, the summaries being published in English, French and German. In this way the pith and marrow of all current medical literature would be extracted and presented in a readable form, but it is to be feared that such a plan is visionary.*

All these devices leave untouched the root difficulty—the immense bulk of raw material to be dealt with. Can this in any way be reduced? This at once raises the question, what prompts doctors to write? Why, as Dr. Johnson wondered of literature in general, have so many people written 'who might have let it alone'? The motives for medical writing are no doubt mixed, some reasonable and creditable, others less so. Good reasons are the necessity for putting on record new observations or results of experiments and the impulse to teach—to impart a conviction or to present a subject in a new light. Bad reasons are the desire for prestige and priority (of which the 'preliminary note' is a familiar example) or the itch for advertisement. In this connection I remember many years ago being present at a meeting of the British Medical Association at which the late Lawson Tait held up a copy of the official organ of that body, saying, 'I divide this journal into the *intra* professional and the *extra* professional advertising portions'. That, of course, was grossly unfair. It is easy to be too censorious in this matter of alleged self-advertisement, for after all the only way in which a young man can let it be generally known by his colleagues that he possesses special knowledge or skill in any department of work is by contributions to the professional journals. Writing from such motives is surely legitimate enough. But one must draw the line at the publication of the same paper in more than one journal and at the equally reprehensible practice of sending out reprints wholesale.

Another motive for writing which is of doubtful validity is the desire for what is nowadays called self-expression—really a form of mental exhibitionism. 'Nobody but a blockhead', said Dr. Johnson, 'ever wrote except for money', yet the number of these gratuitous medical writers is considerable, however difficult it may be for those of us to whom writing is a pain and toil to realize it. How different was it with a member of the surgical staff of the London Hospital in the 18th century, of whom it is recorded that he was 'guiltless of any contribution to medical literature'. No doctor, surely, need desire a better epitaph, for silence, as Carlyle said, is the eternal duty of a man.

These motives being apparently so compelling, there is no need to add temptations and inducements to write—that is simply putting mischief into people's heads. Amongst such uncalled-for inducements I would include all ceremonial orations, all presidential addresses, and in particular all memorial lectures (such as this). The last have multiplied to such an extent as to have become a nuisance, and it is increasingly difficult to find people to give them or to collect audiences to listen to them. In any case there are surely better ways of remembering the dead than by boring the living. But even the total abolition of all extraneous inducements to write would make no appreciable difference to the spate of medical literature, so we are driven to consider what can be done to make it more manageable.

HOW TO CONTROL THE OUTPUT

In the first place, there should be strict birth control in regard to new journals. There being far too many

already, why add to the number? Secondly, amalgamation of existing journals might well be carried out in many cases. It is absurd, to take only one example, that in this country there should be two journals devoted to diseases of children. Thirdly, some journals might be suppressed altogether. Amongst these I would include those which appeal only to a local patriotism such as (let us say) the *John O'Groats Medical Journal* or the *St. Cyprian's Hospital Reports*. There are five of these local journals in England alone and Scotland could add its quota. I am aware of the justifications put forward for their existence—that they get into print work which would not otherwise appear (surely a very bad reason!), that they publish the proceedings of local societies and obituaries of local medical men, that they keep alive a regional patriotism, and so forth, but I doubt if these are adequate. What we should aim at is to have the stream of publications gathered into as few channels as possible. Moreover, superfluous journals lead to superfluous writing, for their editors are sometimes driven to tout for contributions whereas instead of the editor having to woo the writer it should be the writer who has to persuade the editor to find room for his article.

In my view the ideal current medical literature for this country would consist of one good weekly journal catering especially for the general practitioner, which would contain articles mainly clinical in character but also critical reviews and abstracts of the work published in the more specialized periodicals both here and abroad. In addition to this each special branch of medicine would have a journal (but not more than one) appearing at longer intervals, for the publication of original work in that sphere. These journals might also with advantage contain summaries of the more important foreign papers in the specialty. This should meet all the needs both of writers and readers.

STRICTER EDITING

These measures would do something, though not much, to check the flow of superfluous writing, but the chief means to this end must be stricter editing. This would involve, of course, the refusal of many articles which at present find their way into print, but that need cause no regrets, for most of them are better unpublished. Anyone who has to read through large numbers of articles with a view to abstracting from them anything of value must soon be convinced of this. I found, for instance, when doing such work for the *Medical Annual*, that not more than a fifth of the articles sent to me were worth anything—the rest went straight into the wastepaper basket.

Closely involved with this matter of the refusal of articles is the question of payment to writers. It is sometimes argued that an editor cannot look a gift horse in the mouth, but surely if his journal has any right to exist at all there should be competition to get into it; I have been told, too, by a professor in Germany that one reason for the existence of many superfluous medical journals in that country is that they pay their contributors and this tempts to unnecessary writing. Further, the articles which are accepted should be more drastically dealt with. We want more of the severe editing which Langley used to apply in the *Journal of Physiology* when he controlled it. Most articles, for instance, are too long. For that matter almost everything is too long—lectures, speeches, sermons, books. 'Was there ever yet anything written by mere man' (if I may again quote Dr. Johnson) 'that was wished longer by its readers excepting *Don Quixote*, *Robinson Crusoe* and the *Pilgrim's Progress*'?—and some readers would not even expect these. The capacity of the average human being for sustained attention is greatly exaggerated, and in every sphere there is need to practise the art of leaving off. Powerful astringents, it is true, may be required to check the verbal diarrhoea which afflicts so many writers, but it is the business of the editor to administer them. Meanwhile every paper that lends itself to it should have a summary appended

* In leading articles in the *Lancet* (1st April, p. 765, and 5th August, p. 321) some suggestions for the better dissemination of scientific information are fully discussed.

not only that he who runs may read but to facilitate translation of the pith of the paper into the year-books. Fortunately the provision of such summaries is a growing practice.

MEDICAL BOOKS

The over-production of books is as great a nuisance as the multiplication of journals and an even greater expense to libraries. The average doctor is not much of a book buyer, and considering how quickly medical books become out of date one cannot blame him; the only best-sellers in medical literature are textbooks which most students use for examinations, or a few books which have a direct bearing on practice, such as works on therapeutics. But if sales are so small, why are so many books written? The publishers, I think, are largely to blame. In their rivalry with their competitors they easily persuade young would-be authors to write for them. The writer is flattered to be asked and argues that whereas he may get some advantage out of writing the book, he can lose nothing by it; the publisher, on the other hand, recoups himself for his many failures at the expense of the more successful authors. This is a vice inherent in commercial publishing for which apparently there is no remedy. Meanwhile it would be a great gain if, instead of issuing expensive and elaborate textbooks, publishers would provide us with more concise, fully-documented monographs giving a complete account of present knowledge in a limited field, and produced as cheaply as possible. We could also do with more yearbooks.

DULLNESS OF MEDICAL LITERATURE

In considering the quality of medical literature as distinct from its quantity one has to distinguish between its content and its form. As regards the content, one is struck by the great excess of facts and the comparative absence of ideas, generalizations and hypotheses; there is, in short, too much observation and recording and too little reflection. Hence much of it is like a heap of bricks without any mortar to hold them together. The power of wide generalization, of course, is very rare, but medical writers might at least show greater imagination, and the lack of this has the sad consequence that much medical literature is deplorably dull. This dullness is the more curious considering that the subject-matter is so interesting. A medical textbook might well be like one of those omnibus volumes of 'Detection, Mystery and Horror'—for, after all, diagnosis is detection, disease is often mysterious and, heaven knows, our work is full enough of horrors—but, as it is, the average textbook is about as readable as a telephone directory. Take, for instance, the biography of a red blood corpuscle from its birth in the bone-marrow, with its capillary wanderings and its moving adventures by flood and field to its normal gradual old age and burial in the spleen or to its tragic end in a hæmorrhage. It might be made a vivid *Odyssey*, but how dull it all sounds in a textbook of physiology—as arid and sterile, as dry and dusty as the sands of the Sahara. But medical writers are not only afraid of romance, they even fight shy of humour. They seem to think that dullness is expected of them and do not agree with the Virgilian tag that 'in order to speak truth it is not necessary to pull a long face' and still less with the character of Stevenson's who thought that there was 'nothing like a little judicious levity'. And yet it is probably true that a writer has never really mastered his material until he can jest about it; until then it has mastered him. Whilst therefore the volume of medical literature betokens an intense activity of observation and research, its content on the whole is dull and pedestrian.

PROLIXITY AND OBSCURITY

As regards their literary form, medical publications are not—perhaps should not be—literature, if one means by that, as the dictionaries say, 'writings esteemed for beauty of form or emotional effect'.

Brevity, lucidity and a reasonable observation of the rules of syntax are all that can be expected of them; the purple patch is out of place. But these simple demands are often not met. Prolixity and not brevity is too common and is responsible for a good deal of the unnecessary bulk of literature. Lucidity, on the other hand, is to some extent an outcome of the language a writer uses. It is difficult to be obscure in French, easy in German, whilst in the case of English all depends upon how it is written, the man being more important than the medium. In all languages, however, it is probably true that clear thinking and clear writing go together.

Appropos of this, it is one of the unfortunate results of the increasing specialization of knowledge that the writings of workers in one department are often hardly to be understood by those outside it. I confess, for instance, that many papers on medical psychology, biochemistry or iatro-mathematical subjects might, so far as I at least am concerned, just as well be written in Chinese. Much of this obscurity is due to the use of mere jargon, but some of it is unavoidable, for as knowledge extends new terms are needed to embody fresh conceptions. Such neologisms should as far as possible be coined from Greek or Latin roots, despite the fact that Latin is no longer the *lingua franca* of science, but owing to the narrow chauvinism so widely prevalent to-day there is an increasing tendency to use new words of home manufacture. Many of the new Germanisms are of this class. Such terminological self-sufficiency is much to be regretted.

ABSENCE OF LITERARY FORM

In addition to being prolix and obscure medical literature exhibits only too often an absence of any sense of style or even of grammar. American medical literature, although it contains some admirable material, is apt to offend in both these respects. Gould, himself an American, has said of some specimens of it that 'they give shame to gods and men and are fit to arouse the cachinnations of the imps of hell'. We are not yet so bad as that here, but the average of medical writing is probably not so high now as it was last century. Certainly we have no textbooks like those of Michael Foster, Fagge or Osler, and the modern multiple productions which have succeeded them have lost the individual touch. It is noteworthy that much of the didactic writing of older days was in lecture form, the lectures of Trousseau, Graves, Watson and G. W. Balfour are classical examples which spring to mind, that somehow the modern publisher does not favour lectures, although they are usually much more readable than the formal textbook.

There are probably several reasons for so much slovenly writing. Often it is the result of mere haste or carelessness, and the dictaphone, the stenographer and the typewriter have much to answer for in this connection. Medical authors are for the most part not practised writers and should therefore take all the more pains, nor are there lacking plenty of mentors and instructors for the novice both in this country and in America.* To a large extent, however, the root of the evil lies deeper and is a consequence of defective literary and linguistic education. It is deplorable, for instance, that in an examination of the standard of the M.R.C.P. it should have been found necessary to drop Latin and Greek because almost no candidate in recent years ever attempted the comparatively simple translations from these languages, whilst very few show even any knowledge

* For example: Allbutt (*The Composition of Scientific Papers*); Gould (*Suggestions to Medical Writers*); G. H. Simmons and Morris Fishbein (*Art and Practice of Medical Writing*); Maud Mellish Wilson (*The Writing of Medical Papers*); R. D. Gillespie (*The Writing of Medical Papers*, *Guy's Hosp. Gaz.*, May 1930). The M.R.C. 'Notes on the Preparation of Reports for Publication' and the *Lancet's* 'On Writing for the *Lancet*' are also very useful.

of German. The great models of English prose, too, are probably less read by the younger generation, and a literary diet of newspapers, detective novels, and the productions of scenario-writers is no substitute for them.

STYLE AND MATTER

It may be contended in reply to all this that the style of medical writings is not of much importance because these are read primarily for their matter. Unquestionably this is too superficial a view, for, as Allbutt said, 'the man of science ought best to know that style and matter can no more be dissociated than skin and bone; but if we write clumsily, loosely or disjointedly our thoughts are accordingly'.

It is time, however, that I came to an end, or you will accuse me of not practising the brevity which I have preached. Let me therefore conclude with a quotation from Dr. Charles Singer, himself both a scholar and a scientist, in which this question of the relation of form and substance in scientific writing is very clearly presented:

'Humanities and the sciences are far from being as independent of each other as many suppose. If literary studies lead to clear and effective expression and clear and effective thinking in the domain of science, scientific studies ventilate and inform and vitalize literature. The separation of the two disciplines, especially in the adolescent stage of mental development, does an injury to both.'

I believe that to be profoundly true.

Resuscitation

By G. ORGANE

(Abstracted from the *Proceedings of the Royal Society of Medicine*, Vol. XXXV, April 1942, p. 439)

THIS paper by a well-known London anaesthetic specialist was read at a recent meeting of the Section of Anaesthetics of the Royal Society of Medicine. The author's main points were as follows:—

Death on the operating table is due to heart failure, which may be primary or secondary.

Primary heart failure is due to cardiac standstill or to ventricular fibrillation.

Cardiac standstill probably results from vagal inhibition excited reflexly from the respiratory tract or from a painful stimulus elsewhere. The heart may be healthy and will resume its normal rhythm on the application of a suitable stimulus. Overdose of anaesthetic, even of chloroform, produces respiratory failure before cardiac failure.

Ventricular fibrillation is produced by the same stimulus of vagal inhibition, in the presence of an abnormally irritable myocardium. This irritability may be produced by chloroform or cyclopropane and is greatly increased by adrenaline. Adrenaline alone, in very large doses, can produce ventricular fibrillation with other anaesthetics or in the unanaesthetized subject. Vagal inhibition of the normal pacemaker of the heart releases lower ventricular foci of irritability which are not under vagal control, with resultant multifocal ventricular tachycardia leading to ventricular fibrillation. Sudden heart failure under ether anaesthesia is probably never due to ventricular fibrillation except where large amounts of adrenaline have been used.

As adrenaline acts directly on the ventricles it seems likely, even under ether anaesthesia, that intraventricular injection of adrenaline may convert cardiac standstill into ventricular fibrillation.

Burstein, Marangoni, De Graff and Rovenstine (1940) report recovery from ventricular fibrillation in dogs after intracardiac injection of procaine, 5-10 mg. per kilo. in 5 c.cm. of normal saline.

Secondary heart failure is due to anoxia of the myocardium, and occurs with ethyl chloride or chloroform owing to the toxic effect of the anaesthetic.

TREATMENT

This may be preventive or restorative. Preventive treatment, apart from the avoidance of grosser errors, is of little effect in primary heart failure. Restorative measures are likely to be ineffective in secondary heart failure.

PREVENTIVE TREATMENT IN SECONDARY HEART FAILURE

Maintenance of blood pressure.—Where blood pressure fall is due to peripheral vasodilatation, as in spinal anaesthesia, vasoconstrictors may be used (neosynephrine 0.05-0.01 c.cm. or ephedrine 15-30 mg. intravenously). The systolic blood pressure should not be allowed to fall below 80 mg. Hg.

Maintenance of blood volume lost from shock, haemorrhage or transudation of plasma. A systolic blood pressure of 90 mg. Hg. or less due to shock or haemorrhage requires correction. In an early case, intravenous normal saline may suffice. In most cases serum or plasma should be given. Whole blood if necessary after severe haemorrhage or if there was anaemia before operation. Injection of so-called cardiac stimulants may be dangerous in a patient gravely ill from shock or haemorrhage.

Maintenance of oxygen supply.—The supply of oxygen to the blood may be reduced by respiratory obstruction; by too little oxygen in the anaesthetic gases; by deficient pulmonary ventilation; by impaired gaseous exchange (after poison gas or due to pneumonia); by anaemia.

The proportion of oxygen administered may be raised to 30 per cent. If breathing is shallow, artificial respiration or respiratory stimulants should be given. (Carbon-dioxide 5 per cent, picROTOXIN 3 mg., cardiazol $\frac{1}{2}$ -1 c.cm., coramine 1-2 c.cm., or alphalobeline 5 mg., intravenously.) If respiratory exchange is impaired, the oxygen percentage should be as high as possible. Withdrawal of the anaesthetic (or neutralization of barbiturates or avertin by analeptics) is essential.

PREVENTIVE TREATMENT OF SUDDEN HEART FAILURE

Pre-operative atropine or scopolamine to inhibit the vagus; avoidance of chloroform; avoidance of excitement during induction of anaesthesia and of premature operative stimuli; great caution in use of adrenaline, which is absolutely contraindicated with chloroform or cyclopropane.

RESTORATIVE TREATMENT OF PRIMARY HEART FAILURE

(1) Clear the airway and establish artificial respiration with oxygen.

(2) Mechanical stimuli to the heart.

(a) Auricular puncture with any needle of 3½ inches (9 c.cm.) or more in length, piercing the chest wall in the third right intercostal space $\frac{1}{2}$ inch (1.25 c.cm.) from the border of the sternum and passing inwards and towards the mid-line. Irritability to mechanical stimuli is soon lost from anoxia and auricular puncture is less dangerous than delay.

(b) If auricular puncture is not immediately successful, cardiac massage must be started through an upper abdominal wound.

(c) If massage is not effective within four minutes of the onset of heart failure, an incision must be made in the diaphragm and an artificial circulation established by direct massage at a rate of forty compressions a minute.

(3) Adrenaline. If a satisfactory artificial circulation is not established, or if spontaneous contractions have not appeared in ten minutes, inject 0.5 c.cm. of adrenaline 1/1000 solution into the ventricle through the fourth left intercostal space 2 inches (5 c.cm.) from the border of the sternum. By this time, cardiac irritability is reduced and ventricular fibrillation is not likely to occur.

(4) Procaine. If the surgeon attempts cardiac massage and finds ventricular fibrillation, inject into the cavity of the ventricle 10 c.cm. of 2 per cent procaine.

If a satisfactory circulation is not established within four or five minutes, permanent damage to the brain is likely to occur, leading to death at a later period.

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GONI, B. A., DE GRAFF,
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E. A. (1940).

Intestinal Obstruction by Amœbic Granulomata

By J. A. M. CAMERON

CAPTAIN, I.M.S.

and

J. C. COLLINS

MAJOR, R.A.M.C.

(From the *Journal of the Royal Army Medical Corps*,
Vol. LXXIX, September 1942, p. 140)

In considering the ætiology of obstructive tumours of the large bowel the 'Big Three' immediately spring to mind; but besides cancer, tubercle, and syphilis the tropical surgeon may well murmur 'The Big Four' and include amœbiasis under this head.

Since an hypertrophic type of amœbic disease is not common in the intestine itself, it is not usually thought of in making a differential diagnosis in the case of large bowel tumours; but now that isolated cases are being reported in the literature the scant mention of such a condition in the textbooks will no doubt be amended.

CASE REPORT

Corporal E. B., aged 27, was admitted as an acute abdominal emergency; severe pains across the naval area had been present for forty-eight hours, much worse in the twenty-four hours preceding admission, and were associated with vomiting. One profuse vomit twenty hours before we saw him had produced considerable relief. Bowels had not moved for three days.

In the patient's own words, there was 'a feeling of weight between the bladder and rectum for three weeks, with some bowel irregularity, and the occasional passage of blood and slime'. No urinary symptoms and no history of dyspepsia.

Pulse and temperature were normal but the respiratory rate was 30 per minute due to crampy abdominal pains. The patient, although well nourished, was dehydrated; the tongue foul and covered with a brown coating. A tumid abdomen, not rigid, contained no palpable masses, but half-way between the naval and the right subcostal line really acute tenderness was elicited. Auscultation revealed windy peristaltic sounds.

By rectum: One inch above the anus a slightly tender annular swelling, incorporated in the rectal wall, and above this again a firm but not hard mass in the recto-vesical pouch caused us to write 'this mass feels decidedly inflammatory'.

An enema produced a few faecal lumps, but most of it was retained. Immediate examination showed no exudate and no protozoa. Urine was normal. White cells 20,000 per c.mm.

The observation period lasted thirty-six hours, during which pulse and temperature remained normal and there was no vomiting. However, the increasingly windy pains and a spreading area of epigastric tenderness, together with a foul tongue, constipation and an anxious expression, led to laparotomy for intestinal obstruction.

Operation.—An excellent anæsthetic was obtained with spinal and twilight sleep (16 c.c. of 1:1,500 percaine, with patient sitting for thirty seconds).

An exploratory entry by a short upper right paramedian incision revealed abundant clear free fluid and

two masses. One was the size of a normal non-gravid uterus and occupied the rectal ampulla. No adhesions were there; a chain of soft glands ran up the hollow of the sacrum. The larger mass, the size of a tennis ball, occupied the full circumference of the transverse colon. It lay to the right of the midline and corresponded to the area of acute tenderness on clinical examination. It was red and angry-looking, and, on raising the greater omentum, lymph exudate was present on the posterior surface of the mass, which was freely mobile. There were no peritoneal implants, and the swelling was too soft for a carcinoma. More than any other lesion, it resembled Crohn's disease in its acute inflammatory phase.

The whole large bowel was thickened and injected and, proximal to the mass in the transverse colon, it was distended. Resection of this larger tumour was quite feasible, but there still remained the smaller one obstructing the rectum. Therefore we closed the exploratory wound and established a cæcostomy, by withdrawing a pouch of cæcum, suturing it to the peritoneal edge, and wrapping the fundus in vaseline gauze for thirty-six hours. A curved pair of Kocher forceps retained this cæcal pouch in position. Intravenous drip saline was given post-operatively.

On the second day the cæcum was opened under intravenous sodium pentothal (8 c.c.). After profuse foul evacuation a catheter was pushed into the ascending colon and drip saline given. This went on four days and was, in our opinion, responsible for tiding the patient over the most critical period of his illness.

Post-operative course.—During the next month the patient lost weight steadily (170 down to 120 pounds) and ran an intermittent fever which was only temporarily benefited by three five-day courses of sulphapyridine. Investigations which were carried out are as follows: W.B.C., always above 14,000 with a polynuclear leucocytosis. Blood Wassermann and Kahn negative. Blood culture and agglutination against typhoid, paratyphoid, melitensis and abortus groups were negative. Repeated stool examinations were negative for ova, parasites and cysts. Culture gave *B. coli* only. Urine was repeatedly found normal and sterile.

The diet was high-calorie and non-residue in nature, and bulk made up with isogel. Washouts through the cæcostomy were unavailing.

Only when the skin about the cæcostomy became a fungating mass was it realized that the pathological process affecting the underlying bowel had spread to the parietes. The pus from the stoma yielded polymorphus and *B. coli* only. Sigmoidoscopy showed a narrow rectum, with no ulcers, and the instrument was passed for 4 inches only; however, there was an evident anodular condition deep to the mucosa, while foul mucus lay in the rectum.

Emetine was given empirically, with dramatic effect.

After 3 grains had been given, the temperature came down and remained down; 12 grains of emetine hydrochloride were given in twelve days followed by 0.25 gramme of carbarsone b.d. for a month, with the exception of week-ends. The cæcostomy rapidly became clean, then stopped discharging faeces, and finally closed and healed soundly within a month of starting emetine. Thereafter the patient rapidly gained weight and strength. Rectal examinations revealed progressive subsidence in the periproctitis. A barium enema six weeks after discharge from hospital showed no abnormality. The patient is now a fit fighting man.

SUMMARY

(1) An obstructive granulomatous tumour of the large bowel may be amœbic in origin, and may occur at two different sites.

(2) In this case skin involvement first suggested the correct diagnosis.

(3) Emetine may be a most valuable diagnostic drug.

Nutrition and Economic Position of Ceylon

By L. NICHOLLS, M.D. (Camb.)
and

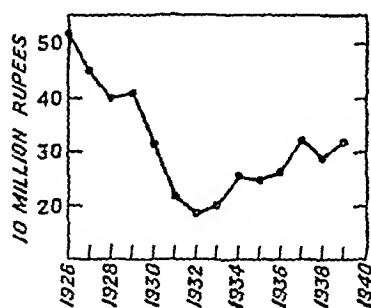
A. NIMALASURIA, M.B. (Lond.), M.R.C.P.

(From the *Lancet*, Vol. II, 19th December, 1942,
p. 734)

THE first nutritional surveys in Ceylon were carried out in prisons and other institutions where clinical signs of malnutrition were found to be prevalent. In the latter part of 1933 and the early months of 1934 similar surveys were done in numerous schools throughout Ceylon. In these early surveys most attention was paid to two signs of dietary deficiency: follicular hyperkeratosis (phrynodema) and 'sore mouth'. The former follows vitamin-A deficiency, and the latter, which includes angular stomatitis and eroded tongue, follows a deficiency of riboflavin. Both were prevalent among the primary school-children—phrynodema in 29 per cent and sore mouth in 8.3 per cent.*

During 1934 and 1935 a severe epidemic of malaria occupied the attention of health officers of the medical department; but from 1936 onwards increasing attention was paid to malnutrition. Qualitative dietary surveys showed that the diets of the poorer classes consisted of parboiled rice and very small amounts of pulses, fish, and vegetables, too highly laced with chillies and other potent currysuffs.

Lectures on nutrition with special reference to local conditions were given to the medical officers, and with the establishment of a division of nutrition in the Medical Department lectures were given to all sanitary assistants and health nurses. Stress was laid on the need for more variety in the diets of the labouring classes and an increase in the consumption of pulses, vegetables (especially green leaves) and fruits; and above all on the need for more milk for children. Public lectures were given and posters displayed. A pamphlet detailing the faults of labourers' diets and the methods of improving these was circulated to every estate superintendent in Ceylon. The subject was taken



Exports from Ceylon, 1926-39.

up in the State Council and large sums of money were voted for a midday meal in schools attended by the more indigent children. There was little doubt that the country was becoming alive to the importance of nutrition, and this was reflected by a great increase of leafy vegetables and other foodstuffs in the urban and rural markets of Ceylon.

About two-thirds of the rice and much of the dried fish and pulses consumed in Ceylon are imported. The production of money crops in preference to food crops may lead to greater prosperity in times of peace but gives rise to a serious hazard in war. Since the outbreak of war the efforts to increase the internal production of foodstuffs have been redoubled and the government has spent much money in bringing this about. Large surveys were carried out in the latter part of 1938 and the beginning of 1939, and again in

1941 and 1942; the results are compared with those found in 1933 in table I.

TABLE I—INCIDENCE OF CLINICAL SIGNS

Year	Children examined	Phrynodema	Sore mouth	Bitot's spots
		Cases and per cent		
1933-34	3,792	1,101 (29.0)	314 (8.3)	..
1938-39	5,184	205 (4.0)	676 (13.4)	91 (1.8)
1941	3,420	18 (0.5)	246 (7.2)	30 (0.9)
1942	3,823	11 (0.3)	78 (2.0)	30 (0.8)

We have carried out parts of the surveys independently since 1934 and the results were consistent.

The economic position in Ceylon must be considered in reference to this astonishing decrease in two signs of malnutrition. The years 1925 to 1927 were boom years and the years 1928 and 1929, though there was a little falling off, were prosperous; but in 1930 there were signs of a slump and in 1931-33 Ceylon was suffering with the rest of the world from a severe economic depression. The figure shows this well. The principal exports are tea, rubber and coco-nuts, and these, having reached a total value of 509 million rupees in 1926, fell to a value of 173 million rupees in 1932. The exports of a country cannot fall in value of 35 per cent of the previous total without all classes of the population being affected in one way or another.

Imports fell more or less *pari passu* with the exports, but the labouring classes are mainly concerned with the imports of foodstuffs. It is necessary to consider the fall in the amounts of foodstuffs which were imported and not their value, because the latter fell during the slump. In 1929 the amounts of rice and dried fish imported into Ceylon were 10.62 and 0.339 million cwt. and these figures fell to an average of 9.63 and 0.307 during the years 1931 to 1933. Amounts gradually rose, and in the last pre-war year (1938) had reached 11.13 and 0.380 million cwt. The fall in the amounts of the imports of foodstuffs had been more than 10 per cent when allowance is made for the growth of the population; with the return of better times these imports increased by about 15 per cent over the slump years.

The value of foodstuffs fell considerably more than the rate of wages. Rice averaged 27½ rupee cents per measure for the first 5 years (1926-30), and from 1932 to 1938 it has averaged just under 16 rupee cents. The price of dhal averaged 21 rupee cents during 1926-30, and afterwards was steady at 13 cents to 1938, and there were similar declines in the values of all other foodstuffs. The rate of wages fell from 10 to 20 per cent, but there was an even greater fall in the value of foodstuffs, being for the more widely used comestibles such as rice, dhal and fish, 30-50 per cent. These falls are shown in table II.

TABLE II—PRICES OF PRINCIPAL FOODSTUFFS AND WAGES

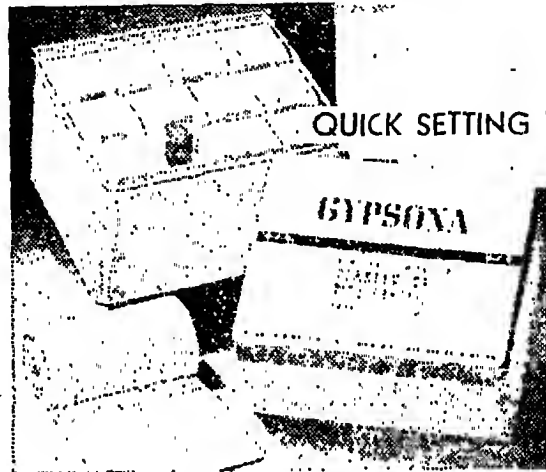
Year	Rice cents per measure	Dhal cents per measure	Dried fish cents per pound	Wages* cents per day
1926-30	27½	21	29	52
1931	21	13	30	52
1932-38	16	13	19	45

* Wages vary in different districts.

* Nicholls, L. *Ind. Med. Gaz.*, 1933, 68, 681; 1934, 69, 241.

G.2

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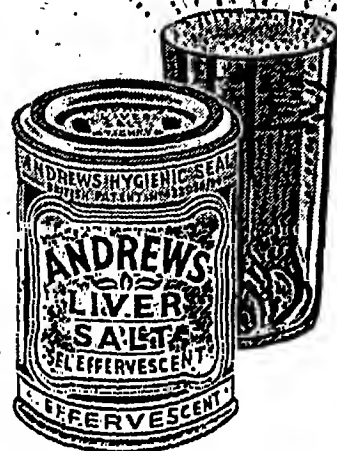


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DISCUSSION

Phrynoderma and sore mouth have been found to be valuable indices of the prevalence of malnutrition among the school-children in Ceylon. The considerable fall in recent years in the prevalence of these signs has followed activities by the Medical Department to make people mindful of nutrition, a midday meal to the more indigent children, efforts by the Agricultural Department to encourage a far greater production of foodstuffs within the country, and the appearance of increased amounts of more approved types of vegetables in the market. Equally, however, the fall has followed improved economic conditions, and, as the first surveys were made just after the depression, the prevalence of signs of malnutrition then found was probably due to the depression.

It is impossible to decide how much of the improvement in nutrition of children has been due to direct action by various departments and how much has followed improved economic conditions; but it seems likely that economic improvement has played the greater part. This does not imply that the medical efforts are not of great importance.

The war has come nearer to Ceylon, and strict rationing has been introduced. The state of nutrition of the labouring classes will be watched by repeated inspections of school-children for phrynoderma, sore mouth and other signs. Signs of dietary deficiency which have been found valuable in nutritional surveys in the tropics will probably also be useful in assessing the state of nutrition of the people of the distressed countries of Europe.

A Simple Medium for the Isolation of *B. dysenteriae*

By T. B. GALLIE

(Abstracted in the *Bulletin of Hygiene*, Vol. XVII, September 1942, p. 656, from the *Journal of Pathology and Bacteriology*, Vol. LIV, April 1942, p. 256)

LEIFSON'S medium is highly satisfactory for the isolation of dysentery bacilli but is tedious to prepare, and the necessary pork may be difficult to obtain. In the medium now described some of the substances employed by Leifson have been used to modify MacConkey's medium:—

Peptone (Parke, Davis)	20 gm.
Sodium desoxycholate	5 "
Sodium citrate ($\text{Na}_2\text{C}_6\text{H}_5\text{O}_7 \cdot 2\text{H}_2\text{O}$)	21 "
Ferric-ammonium citrate (green scales)	2 "
Lactose	10 "
Distilled water	1,000 c.c.

Add the peptone, desoxycholate and sodium citrate to the water, dissolve in the steamer, adjust to pH 7.4. Add 25 gm. of agar powder, steam for 20 minutes, filter through Chardin paper or cotton-wool. Add the lactose, previously dissolved in a little water and sterilized, and the ferric-ammonium citrate. Sterilize by exposure to 100°C. for 20 minutes on each of three successive days. When pouring plates, melt the medium and to each 100 c.c. add 0.3 c.c. of a sterile 1 per cent aqueous solution of neutral red.

Good results were obtained in the plating of artificial mixtures of dysentery bacilli and *Bact. coli*, and 166 faecal specimens from suspected cases of dysentery were then examined. On Leifson 102 were positive for *Bact. flexneri*, 100 on the modification, and 63 on MacConkey: 14 were positive for *Bact. sonnei* on Leifson and the modification, against 10 on MacConkey. Stools taken later from 30 unselected cases gave no positive results on MacConkey, whereas 11 were positive both on Leifson and the modification.

Paracolon bacilli grow on the medium, but the colonies can usually be recognized by their brownish centre.

J. C. CRUICKSHANK.

Reviews

REGIONAL ANALGESIA FOR INTRA-ABDOMINAL SURGERY. WITH SPECIAL REFERENCE TO AMETHOCAINE HYDROCHLORIDE.—By Norman R. James, L.R.C.P. & S. (Edin.), D.A., R.C.P. & S. (Eng.). J. and A. Churchill, Limited, London. Pp. vi plus 57, with 27 illustrations. Price, 6s.

DR. JAMES is to be congratulated in giving to the medical profession such a clear and concise description of his method of regional analgesia, covering in some detail the pharmacology and dosage of the drug employed, the selection, preparation and premedication of the patient, including his graphic account of how to perform bilateral intercostal block, bilateral posterior splanchnic block, paravertebral lumbar block, unilateral or bilateral and, if necessary, caudal block or bilateral transsacral block—a tedious process, as he describes it—as well as the method of blocking the nerve roots from the opposite side in unilateral procedures, ilio-hypogastric and ilio-inguinal nerve block for appendicitis, and the necessary block for the skin incision, also a suitable block for suprapubic drainage. In short, to anaesthetize a woman with the differential diagnosis of acute appendicitis, acute cholecystitis or an acute tubal infection, would necessitate giving some twenty or thirty injections, not including premedication, intravenous barbiturate and a light inhalation anaesthetic.

Nevertheless, this little book is full of practical points which will be of interest to the majority of anaesthetists and surgeons. For instance, the importance of basing the dosage of all local anaesthetics upon the body-weight, taking into account such things as the metabolic rate, the presence of excess fat and large avascular abdominal tumours. A case was recorded recently, in which an overdose of nupercaine (by infiltration) was given, due to the presence of a large ovarian tumour; the importance and the delicate nature of adrenaline is stressed; also the antagonism which exists between the *p*-amino-benzoic acid derivatives and the sulphonamide drugs; due emphasis is given to the use of oxygen therapy before, during and after operation in the seriously ill and shocked patient, and it will be the experience of the majority who have anaesthetized air raid and battle casualties, that shocked patients respond well to oxygen given through a B.L.B. mask, but when they arrive in the theatre and can be given full oxygen, preferably under pressure, they will improve by another twenty-five to fifty per cent.

The paragraphs upon the examination and selection of patients, and the temperament of surgeons will be of value to most anaesthetists, as the patient's attitude to the operation, and particularly to the anaesthetic and anaesthetist, is not sufficiently stressed. Mutual confidence between patient, surgeon and anaesthetist goes a long way towards the successful conclusion of what is, to the patient anyway, a milestone in his life.

Premedication figures largely in Dr. James' technique and the intravenous method has much to commend it and is accurate in suiting the dose to the individual, the essential feature of success; there would appear to be, however, considerable risk of overdose by this method in inexperienced hands.

There is however much to be criticized in this volume. To achieve success in this type of analgesia, a dose of the selected drug is given which approximates closely to the minimal lethal dose, and yet some two-thirds of this dose is wasted: as Dr. James remarks, 11.5 c.c. is injected into each intercostal space in the hope that 3 or 4 c.c. will reach the nerve and produce effective analgesia. This method would appear, therefore, to be inaccurate, wasteful and quite possibly dangerous, not to mention the pin-cushion like appearance of the patient, on completion of the technique. Compared with high spinal block, for instance, where all the advantages claimed by Dr. James obtain—splanchnic block, sensory and motor paralysis, quiet

respirations and negative intra-abdominal pressure, and even the disadvantages—pallor, sweats, nausea and vomiting, and the small degree of anoxia following the fall of blood pressure, which invariably occurs with splanchnic block—the patient receives only one prick after premedication, and the maximum dose of the drug, in the case of nupercaine (1 in 1,500), is ten times smaller than the minimal lethal dose.

In fact, in the paragraphs on 'Toxic effects' and 'Attention to the patient during operation', it would appear that Dr. James is not quite clear which symptoms he mentions are due to overdose of the drug used, and which are the result of anoxia following the fall of blood pressure. It would be interesting to know what fall of blood pressure actually occurs in this method and in what degree it differs, if any, from that one expects following a subarachnoid block to the same thoracic level.

In his treatment of toxic effects, Dr. James gives the impression that intravenous pentothal is the treatment *par excellence*, but there is much to be said for the view that this is entirely unnecessary unless convulsions are present: the Trendelenburg position and artificial respiration with oxygen through a clear airway are the essential features of successful treatment. Intravenous pentothal has been used empirically to control the convulsions of overdose of local anaesthetics, but such use is both unphysiological and dangerous.

Regarding the post-operative period, it is true to say that these patients are in happier condition than those who have had general anaesthesia with toxic drugs such as ether or chloroform, but Dr. James is scarcely correct in saying that they can be put straight back to bed in the Fowler position and that they require less attention. Such patients require to be flat, until all the effects of the drug have worn off, at least three hours, and during this time they cannot look after themselves. No mention is made at all of post-operative pulmonary complications, which, according to King, are most frequent following local anaesthesia.

In its application to war surgery, this is certainly not a method which could be used with any degree of success in forward areas, although theoretically it has much to commend it. Practically, in this country (India) anyway, lack of water supply, lack of time, risk of infection with multiple injections, etc., would contra-indicate its use. Also, most battle casualties are suffering from some degree of shock and are easily anaesthetized with intravenous pentothal and/or ether, both of which methods are safer and simpler than regional analgesia.

Finally, it is to be wondered upon what grounds Dr. James bases his extraordinary statement that 'in grave cases, and especially in severe degrees of shock, there is a better chance of ultimate recovery if a general anaesthetic . . . is avoided altogether. The very act of rendering a critically ill patient unconscious . . . brings into play injurious factors, which are beyond the control of the anaesthetist'. This is not the experience of others, and it is entirely unsupported by any facts to prove its truth.

The printing and layout of this book are good and there is only one printing error. There are also some useful photographs and diagrams, illustrating the details of technique.

In conclusion, although this is an interesting little book in many ways, there is scarcely sufficient evidence, at present, to recommend regional analgesia for abdominal surgery, in preference to the simple and safe methods of inhalation, intravenous and spinal anaesthesia in current use.

J. R. B.

A SHORT TEXTBOOK OF MIDWIFERY.—By G. F. Gibberd, M.B., M.S. (Lond.), F.R.C.S. (Eng.), F.R.C.O.G. Third Edition. 1943. J. and A. Churchill Limited, London. Pp. ix plus 542, with 195 illustrations. Price, 21s.

SINCE the appearance of the first edition in 1938, the discerning practitioner or student of obstetrics has looked forward with eagerness to the publication of

each fresh edition of this work. It is therefore no mean appreciation of the book to state that the 1943 edition satisfies expectations.

Originality marks both the illustrations and the text. Amongst the most interesting chapters are those dealing with the development of the ovum, the management of normal pregnancy, the toxæmias and diseases associated with pregnancy and asphyxia neonatorum.

Much more could perhaps have been written on the injuries of the new born and the causes of foetal death and neonatal death, since in the past ten years attention has been closely focussed upon the stillborn infant and upon the causes of neonatal death. The author has however provided two very readable chapters on this form of vital loss which may serve to stimulate systematic investigation in our maternity institutions. An excellent textbook.

L. G.

A HANDBOOK ON DIFFICULT LABOUR.—By M. L. Treston, F.R.C.S., F.R.C.O.G., Colonel, I.M.S. Second Edition. Published by the author. (Address: Inspector-General of Civil Hospitals, Burma, Simla.) Printed at Liddell's Printing Works, Simla. Pp. 135. Illustrated. Price, Rs. 5

It must be borne in mind that Colonel Treston is offering not a textbook on midwifery but a handbook on difficult labour. As such, the book should offer considerable field for study by both the young obstetrician and the medical under-graduate.

The chapters on bleeding, *viz.* hæmorrhage in late pregnancy, placenta prævia, and post-partum hæmorrhage, are well handled and contain much useful information presented in a direct and unambiguous manner.

The illustrations have suffered from rather indistinct printing for which war conditions are presumably responsible. The book is well worth the modest cost cited.

L. G.

CANCER OF THE UTERUS.—By Elizabeth Hurdon, C.B.E., M.D. 1942. Oxford University Press, London. Humphrey Milford. Pp. xii plus 188. Illustrated. Price, 17s. 6d. Obtainable from Oxford University Press, Bombay and Calcutta

THIS small book is a treatise on the subject of carcinoma of the uterus, as envisaged by the Staff of the Marie Curie Hospital in general, and by Dr. Hurdon in particular. The author has impartially reviewed the many existing theories of the causation of cancer, but seems herself to incline to the view of a hereditary diathesis plus a secondary factor.

An extensive statistical review has been prepared, and is supported with many tables showing the operability rate and the mortality rate of cases treated in many parts of the world. Surgery versus Radiotherapy and Surgery plus Radiotherapy have been contrasted, and the result correlated, with a distinct trend in favour of the latter which is in keeping with contemporary thought and practice.

The special technique of the Marie Curie Hospital for the application of the radium into the uterus and cervix is fully described; it however differs little from the established method of the Stockholm School.

When discussing the method of making biopsies, Dr. Hurdon makes a statement which calls for comment. She states that she never encroaches on normal tissue when making a biopsy, but merely takes a portion of central part of the growth away by means of a loop or other such instrument. This is sufficiently at variance with the orthodox method to call for comment. It is known that a few eminent pathologists, amongst whom is Sampson Handley, favour this method described by Dr. Hurdon, but the vast majority of surgeons and pathologists consider that it is so open to misconstruction that they will have nothing to do with it.

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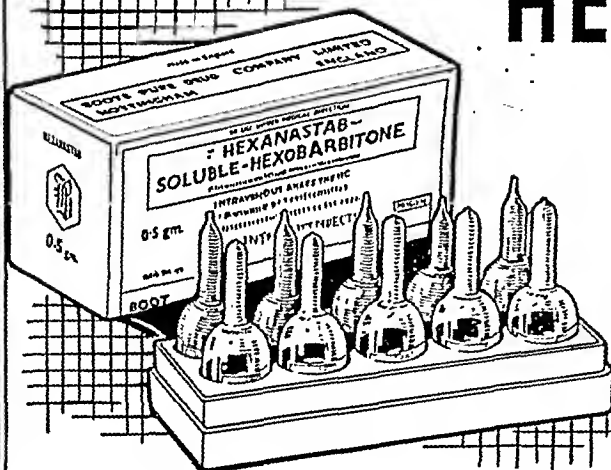
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H. E. M.

FORENSIC MEDICINE: A TEXTBOOK FOR STUDENTS AND PRACTITIONERS.—By Sydney Smith, M.D. (Edin.), F.R.C.P. (Edin.), D.P.H. Eighth Edition. 1943. J. and A. Churchill Limited, London. Pp. xii plus 660, with 179 illustrations. Price, 28s.

THIS edition rapidly follows the revised edition by John Glaister, both books being the products of the Scottish school, which, of late years, has done so much to keep British forensic medicine in the front rank.

The author has brought up to date the changes in the Poison and Pharmacy Act as well as the list of industrial diseases under the Factories Act and the Workmen's Compensation Act.

Every doctor or policeman, who has to work in India, is constantly faced with cases of murder either by violence or by poisoning. His library will not be complete unless he has such an up-to-date book for ready reference. Amongst the books on the laboratory bench of the toxicologist, Sydney Smith will always be found close to Witthaus. The book has now far outstripped the requirements of the present-day overworked medical student.

In chapter IX, wounds from firearms and the examination of projectiles are exceedingly well discussed, and the diagrams are clear; if history repeats itself, the subject-matter will often have to be consulted in the years following the cessation of the present hostilities.

The author has added an appendix (IV) of only nine pages on forensic medicine in the East. It is suggested that in future editions more importance should be attached to this section, even if it be necessary to call in an Indian collaborator. The few books that are now produced in India are out of date, so there is great scope for a reliable book that will embody some of our medico-legal problems. Its circulation in the East would then probably rival that in the West.

The book, as it stands, is one of the most outstanding of its kind in the English language, and will bear most searching use.

The publishers have produced a very fine edition, well up to their pre-war standard, at the modest increased cost of only twelve per cent.

D. R. T.

MEDICAL DISEASES OF WAR.—By Sir Arthur Hurst, M.A., D.M. (Oxon.), F.R.C.P. Edward Arnold and Company, London. Pp. viii plus 495. Illustrated. Price, 21s.

THE following are quotations from the preface to this third edition. 'This third edition of *Medical Diseases of War*, the sixth edition of the book originally published in 1916, has been brought up to date with the help of all the literature available up to August 1942. New chapters have been added on typhus fever and on diphtheria. The former is written by Dr. Melville D. Mackenzie, whose experience of the disease in all parts of the world is unique among British physicians. Dr. E. H. R. Harries has written the chapter on diphtheria, which has proved to be one of the major medical problems in the Middle East.'

'The most important additions to this edition apart from those already mentioned are in connection with the treatment of bacillary dysentery with sulphaguanidine, the probable occurrence of trench fever before and since the war of 1914-18, new methods of isolating enteric and dysentery organisms, the incidence, pathology and treatment of infective hepatic jaundice, the diagnosis and treatment of cerebral concussion, Mellanby's work on the aetiology and treatment of scabies, and that of T. J. Phillips and of Ida Mann on the delayed action of mustard gas on the eye.'

The chief feature of this edition as of previous editions is the discussion of war neuroses which occupies the first 168 pages, nearly one-third of the book. The rest of the book is taken up by sections on the following subjects—digestive disorders in soldiers, effort syndrome, trench fever, louse-borne typhus fever (by Melville D. Mackenzie), typhoid and paratyphoid fevers, dysentery, epidemic jaundice, malaria (by Colonel H. B. F. Dixon), meningococcal fever (by Major-General A. W. Scott), diphtheria (by E. H. R. Harries), tetanus, war nephritis, skin diseases in war (by H. W. Barber), and gas poisoning.

The section on gastric disorders which has proved to be such an important problem of the army in this war, much more than in the last war, is of much interest. The section of effort syndrome is also good.

The other sections, which vary in length from 16 to 40 pages, give good résumés of their subjects.

The whole book however strikes one as lacking balance. It is a compilation, and a useful one, but it does not hang together as a comprehensive and carefully planned account of the medical diseases of war. To produce such a book in war time is difficult or impossible, so probably the best that can be done is to modify and bring up to date this book which dates back to the last war.

Sir Arthur Hurst's account of war neuroses, based on experience during and after the last war, is very well known and unique in its way. It would be interesting to know to what extent and in what ways experience of war neuroses in the present war has differed from that in the last war. This book does not give us much information on this point.

J. L.

THE ESSENTIALS OF MATERIA MEDICA, PHARMACOLOGY AND THERAPEUTICS.—By R. H. Micks, M.D. (Dub.), F.R.C.P.I. Third Edition. 1943. J. and A. Churchill Limited, London. Pp. x plus 426. Price, 16s.

THE book which has been revised and brought up to date in the present edition, is meant for the student and practitioner of medicine. Only those drugs which are of real therapeutic value have been described. All doubtful and controversial matters have been eschewed. Except two minor defects, *e.g.* the omission of disinfectants, admittedly a complex subject, and the absence of a few diagrams illustrating the site of action of drugs (these would have enhanced the value of the book for teaching purposes), it is a most suitable textbook of the subject for the medical school students. The actions and uses of drugs have been presented clearly and in a manner which makes it easy for reader to learn and retain. The young practitioner will find the prescribing hints very useful and instructive. The senior practitioners who want to renew their knowledge of the subject will find this brief treatise on modern pharmacology a most informative and pleasant book to read. In short, we can unhesitatingly recommend the book to the student and practitioner alike as the most useful concise book on the subject published in recent years.

J. C. G.

RECENT ADVANCES IN PATHOLOGY.—By G. Hadfield, M.D., F.R.C.P. (Lond.), and Lawrence P. Garrod, M.A., M.D., B.Ch. (Camb.), F.R.C.P. (Lond.). Fourth Edition. 1942. J. and A. Churchill Limited, London. Pp. viii plus 346, with 35 illustrations. Price, 18s.

THIS book has reached us with a note from the British Medical Information Service by M. J. Stewart, Professor of Pathology, Leeds University, for the guidance of reviewers, and it is stated that this note may be published as it is, or in a modified form. This is reviewing made easy, possibly too easy, and the present reviewer's first reaction was probably that of any other reviewer who takes his job seriously, namely that of antagonism to this procedure, which could

obviously be abused. The reviewer decided therefore to write his own review, but, after carefully reading through much of the book, he has decided that Professor Stewart's notes are better than anything that he could produce himself, and that the high praise that is given to this book is amply justified in every way. One point which Professor Stewart has not emphasized is the attractive way in which the material has been presented; the writers have a way of making their matter really interesting. The reviewer has read parts of this book on buses and on trains, and on two occasions he almost overshot his destination. Two small criticisms of the writing may be offered. Although the writing is very clear, freer punctuation of certain sections would have improved them. The common mistake of calling night blindness 'hemeralopia' is made in this book.

The following are the main parts of Professor Stewart's notes :—

'Nearly two decades have elapsed since the English medical publishing house of Churchill began to bring out what they happily named their "Recent Advances" series. Gradually the field covered by these invaluable manuals has been extended until now practically all branches of medicine are included. The volumes are of handy size—manuals in the strictest sense of the term—and all of them are by well-known British teachers and investigators. That there was a real need for such a series in the English-speaking world is shown by the frequency with which new editions have been called for, and they are equally popular with students, teachers and practitioners of medicine.'

'One of the most successful of the series has undoubtedly been "Recent Advances in Pathology", now in its fourth edition. The authors are Professor of Pathology and Professor of Bacteriology at St. Bartholomew's Hospital, London, and they have been responsible for all four editions. In their preface to the first edition (1932), they gave as their conception of the main purpose of the volume the presentation of recently acquired knowledge of disease processes in a form useful to the student of medicine. To this end it seemed inevitable that they should deal with specific diseases rather than with the more abstract problems which underlie them, and it was equally obvious that, if the book were to be of a reasonably small size, only a certain number of main subjects could be dealt with in any detail. In the choice of material and in the fullness of its treatment the authors were guided by three main considerations: the intrinsic importance of the subject, the extent of its illumination by recent work, and the degree of availability of such new information in other literature.'

'In each successive edition new chapters and new sections have been introduced, while chapters and sections of the previous edition have been deleted. In each instance the changes effected have been extensive, the authors' chief aim being to deal fully with a restricted range of those subjects whose study has made important progress in the intervening period. The result is a series of volumes which are complementary to one another, and only to a limited extent overlapping.'

'The principal topics discussed in the new edition are inflammation and infection, the reticuloses and reticulo-sarcomata, experimental cancer research, vitamin deficiency diseases, rheumatic endocarditis, arterial hypertension, pneumonia, nephritis, gastro-intestinal diseases, especially in their relation to anæmia, and diseases of the ductless glands. This last chapter has been contributed by a clinical colleague of the authors, Dr. E. F. Scowen.'

'In the chapter on inflammation, Menken's work is fully and critically reviewed and there is a good account of the Duran-Reynal's phenomenon. The chapter on the reticuloses and reticulo-sarcomata includes short but clear and up-to-date accounts of the lipoidoses, Schaumann's disease, and regional ileitis. The three chapters on experimental cancer research include sections on chemical carcinogenesis, the filterable fowl tumours, tumour metabolism, immunity to transplanted

tumours, the influence of heredity and the "mother's milk" factor of Bittner. Vitamin deficiency diseases are dealt with in a very satisfying manner, with full consideration of vitamin K and its relation to the prothrombin content of the blood and to hæmorrhagic states resulting from prothrombin deficiency.

'Chapter IX provides a good and impartial discussion of the various ætiological theories of rheumatic fever and it is concluded that "more progress has been made towards identifying hæmolytic streptococci as the cause of this disease than in any other direction". It remains to be explained "why these organisms behave so differently, or why the body reacts to their presence in so different a way, from anything to be seen in other streptococcal infections".'

'The chapter on Bright's disease includes an important and topical section on renal failure and ischaemic necrosis of muscle, compression-anuria and the "crush syndrome", and another on extra-renal azotæmia. In the chapter on the ductless glands, first place is given to the sex hormones, the pathology of the adrenal cortex, and necrosis of the anterior lobe of the pituitary and its relation to Simmonds' disease.'

'The volume is thoroughly well documented and there are full subject and author indexes. Teachers of pathology as well as their pupils will find it of the greatest value as a labour-saving method of keeping abreast of recent pathological discovery.'

J. L.

RESEARCHES IN CLINICAL PHYSIOLOGY.
VOLUME II.—By Sir Almroth E. Wright, M.D., F.R.S. 1943. William Heinemann (Medical Books), Limited, London. Pp. vii plus 163. Price, 12s. 6d.

This is volume II of these researches. Volume I deals with pathology and treatment of war wounds and of their infections. The present volume deals with quite a different range of subjects, such as making milk suitable for diabetics, infants and invalids, studies of the coagulation of the blood, scurvy, artificial respiration, chilblains, thrombosis in typhoid fever, tests of kidney efficiency, hæmophilia. In all about two dozen papers or excerpts from papers published between 1891 and 1905 are included in the present volume. Many of these papers are of historical interest. Some of them serve to remind us what great advances have been made since these papers were written.

The name of the author is famous throughout the world, and medicine owes much to him. We do not know precisely what object the reprinting of these papers is intended to serve, particularly in these times of paper shortage. They were published in journals and books which are readily available in all good medical libraries.

The book is excellently printed.

J. L.

DISEASES OF THE NERVOUS SYSTEM: DESCRIBED FOR PRACTITIONERS AND STUDENTS.
—By F. M. R. Walshe, O.B.E., M.D., D.Sc., F.R.C.P. (Lond.), Hon. D.Sc., Nat. Univ., Ireland. Third Edition. 1943. E. and S. Livingstone, Edinburgh. Pp. xvi plus 350. Illustrated. Price, 15s. 7d.

This is the third edition of this book within three years. It is a most excellent book and admirably serves the purpose for which it is written. It covers very well the knowledge of the disease of the nervous system which should be possessed by the medical student and the practitioner.

To cover such a large subject within such a relatively small compass is a great achievement, and necessarily the treatment of individual diseases has to be brief. It would have been of help if some indication had been given of where more exhaustive surveys of the different subjects could be found; the book contains no references and not even a select bibliography.

J. L.

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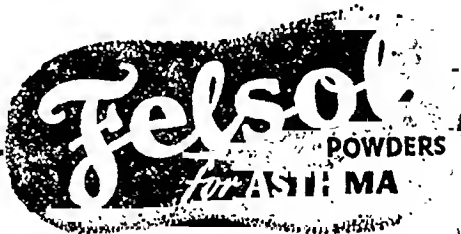
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Correspondence

A. STEPHENSI AND MALARIA IN CALCUTTA

SIR,—In 1932, Covell conducted a malaria survey in Calcutta, and discussed the epidemiology of the disease in this city. He reached the following important conclusions:—

- (i) The amount of endemic malaria in the city was, at that time, slight.
- (ii) Transmission of the disease definitely occurs, probably originating chiefly from imported cases, leading to localized outbreaks in various parts of the city.
- (iii) *Anopheles stephensi* is undoubtedly the transmitting agent of the disease in Central Calcutta.

The last opinion, shared by other authors, was based on a study of a wealth of information collected by many earlier workers. Since 1932, no further knowledge has been gained which suggests a revision of that opinion. On the contrary, it is confirmed by findings which are reported in this preliminary communication. But the information available until now has provided evidence entirely of an indirect nature, for in the long history of the scientific study of malaria in Calcutta, which city may well claim to be the birth-place of the science of malariology through the great discovery of Ross made within its boundaries, only 285 *Anopheles stephensi* appear to have been dissected, all under Senior White (1940), between April 1937 and March 1940. Not a single specimen proved positive for malaria infection, either of the gut or of the glands.

Within the last twenty months, at least two factors have possibly operated, and are continuing to operate, towards a complete reversal of the malaria problem in Calcutta. One was the arrival last year in the city of large numbers of evacuees from Burma, carrying malaria acquired in the most tragic circumstances during their trek through the extremely malarious territories of Burma and Assam. The other factor is the acute food problem now prevailing in the province of Bengal, notably with regard to rice, the staple diet of the people, of whom numbers are coming to Calcutta from highly endemic districts in search of food and employment. Thus the danger to the presumably susceptible, indigenous population of Calcutta has increased, and would have done so enormously, but for one mitigating factor, that the vector feeds mainly on cattle.

During the present year, I have encountered several cases of malaria undoubtedly acquired in central Calcutta. In instances, most of the children and young adults in a family have been struck down, one after the other, all or the majority showing infection with the same species of malaria parasite. Such cases have been found both among persons who have never been out of Calcutta, and among others who have not experienced malaria before coming to Calcutta. The writer was recently informed of an outbreak of malignant malaria, last year, among in-patients in the Carmichael Hospital for Tropical Diseases; evacuees from Burma, suffering from malaria, had shortly before that been admitted into the hospital. At the time of writing, information suggests that transmission is occurring in a certain orphanage; this is being investigated.

Thus, convinced from personal experience of the fact of malaria transmission in central Calcutta, I began a search for infected *Anopheles* in July of this year. The search is being conducted in houses in which transmission is believed to have occurred recently, or is taking place now, and in one other house which has previously yielded, and is yielding, a fairly good number of *Anopheles stephensi*, but which has never been known to harbour a case of malaria though its occupants are normally resident in Calcutta. I cannot avoid commenting on the sharp contrast between my experience

and that of other workers in the matter of the collection of my adult *Anopheles stephensi* in Calcutta. In 1940, Senior White closed his investigation on *A. stephensi* because the mosquito had 'become so rare in Calcutta as to make the cost of collection prohibitive'. In a search of 20,564 houses, his collector obtained only 111 female *A. stephensi*, while 13 were caught in a cow-shed; a further 170 were caught in a cow-trap as against 3 in a man-trap. The total catch in 28 months' search amounted to 297 females of *A. stephensi*. This difficulty of obtaining adults lies behind the paucity of the dissections of the species. In 1938, I personally collected 249 females of the species from a single bed-room during 4 months from May to August; these mosquitoes were subjected to the precipitin test (Roy, Chandra and Siddons, 1938). This year, 32 females have been obtained during the month of July, from 5 houses. As the day-time resting places of *A. stephensi* are still unknown, it is difficult to offer any explanation for these divergent experiences.

Of 28 mosquitoes dissected, so far, in the present investigation, one has been found with gland infection. As the *A. stephensi* problem has been complicated by the separation of races by Sweet and Rao (1937), the mosquitoes are being conserved for race determination by egg measurements prior to dissection. The infected mosquito is among those which have deposited eggs; these have been measured and the number of maxillary teeth also recorded. These findings are of sufficient interest to justify publication at this stage of the investigation.

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L. B. SIDDONS.

DEPARTMENT OF PROTOZOOLOGY,
 SCHOOL OF TROPICAL MEDICINE,
 CALCUTTA,
 4th August, 1943.

NEED OF INDUSTRIAL MEDICAL ORGANIZATION

SIR,—Industry in India today is not falling behind other countries, especially in these days of war. With this advancement industrial hygiene is drawing the attention of the medical profession, government, and proprietors. In other countries much has been done to this end by framing definite rules and regulations, and a special branch of industrial medical science has developed, but in India, industrial medicine is still unknown to many.

Very few companies look after the health of the workers. They ignore the aims of industrial hygiene, as stated by Napier in March 1942 issue of *Indian Medical Gazette*, (1) the prevention of immediate ill effects of certain occupations on the industrial workers, and (2) the maintenance of the mental and physical health of the worker at its high level, so that his or her output is maximal.

It must be understood that the ill effects of certain occupations are related to the personal hygiene of the worker, but the other aim, namely the efficiency of the worker, must be maximal is the direct concern of the employer. Government also wants the maximum production in the factories in these days of war. But to attain this, the health of the workers must maintain its high level which will not be possible if the proprietors and government ignore the importance of industrial hygiene.

Recently the Government of India has issued some questionnaires to the public relating to the health insurance scheme of the factories; but that is not sufficient

for the purpose. By appointing a panel of doctors or by engaging whole-time medical officers in factories much cannot be achieved. A separate organization must be formed to study the various problems of industrial medicine and to help the government by its advice in this direction.

It is also high time that the medical profession of India should be conscious of this side of medicine and should take the initiative in this direction.

CHARU CHANDRA KARKOON,

L.M.F., L.T.M.

Medical Officer.

MAHALUXMI COTTON MILLS,
PALTA,
24-PARGANAS.

PREVALENT TYPES OF CHOLERA VIBRIO

STR.—Out of 250 cases of cholera (diagnosed on clinical grounds) in 1941 *Vibrio cholerae* Inaba sub-type were isolated in 71 and *V. cholerae* Ogawa sub-type were isolated in 76 and no vibrios seen in 58.

Two hundred and twenty-six cases were examined in 1942 and *V. cholerae* Ogawa were found in 70 and *V. cholerae* Inaba in 45, and no vibrios were seen in 111. This 45 includes 9 cases out of 14 evacuees from Burma.

Two hundred and sixty-six cases of cholera were examined in 1943 (up to 10th July, 1943) and *V. cholerae* Ogawa were isolated in 154 and no Inaba sub-type could be seen at all this year. No vibrios were found in 112.

Eight hundred and fourteen samples of stool were examined from these 266 cases.

A consideration of these findings is important in the preparation of prophylactic vaccine. *V. cholerae* Ogawa only has been found in 1943 and isolations of *V. cholerae* Inaba have been gradually declining since 1941. So *V. cholerae* Ogawa should be in greater proportion in the vaccine and only a small amount of *V. cholerae* Inaba may be added to the vaccine for inoculations in Calcutta. I had been to Madras in March this year, and found that only *V. cholerae* Ogawa were isolated during cholera epidemic there this year.

In future, too, great care should be taken to type the vibrios isolated during epidemic and to supply the appropriate prophylactic vaccine.

S. K. SEN GUPTA.

M.B., D.T.M.

Officer In-charge.

BOWEL DISEASE RESEARCH
DEPARTMENT,
SCHOOL OF TROPICAL MEDICINE,
CALCUTTA,
10th July, 1943.

[Note.—Since this letter was received, the writer has informed us that in one case recently *V. cholerae* Inaba was isolated.—EDITOR, I. M. G.]

Service Notes

APPOINTMENTS AND TRANSFERS

LIEUTENANT-COLONEL R. McROBERT is appointed temporarily to officiate as Civil Surgeon, New Delhi, with effect from the forenoon of the 29th May, 1943.

Lieutenant-Colonel F. H. Whyte is appointed Civil Surgeon, Simla West, with effect from the forenoon of the 31st May, 1943.

Captain J. H. Caverhill, Staff Surgeon, Murrec, assumed charge of the office of Civil Surgeon, Murrec, in addition to his own duties on the 22nd June, 1943, relieving Captain D. H. Harrison, transferred.

INDIAN LAND FORCES

INDIAN MEDICAL SERVICE—SECONDED TO INDIAN ARMY MEDICAL CORPS (Emergency Commissions)

The undermentioned officers are transferred to the General Service Cadre, with effect from the date specified:—

Captains

B. R. Shanm Rao. Dated 1st June, 1943.
S. C. Majumdar. Dated 12th June, 1943.
I. M. Bauerjee. Dated 19th June, 1943.
T. R. Krishnamurthy. Dated 11th June, 1943.
M. A. R. Azhar. Dated 3rd July, 1943.

Lieutenant

A. R. Anantharaman. Dated 8th June, 1943.

To be Captains

William Bernard Roantrec. Dated 4th May, 1943.
Trilok Singh Chand. Dated 5th March, 1943.
Profulla Koomar Das. Dated 23rd April, 1943.

7th May, 1943

Sisir Kumar Mitra. Nand Kishore Prasad Sinha.
Bindiganavale Raghavan. Dated 9th May, 1943.
N. Gangadharan. Dated 13th May, 1943.
V. C. C. F. J. Faria. Dated 6th February, 1943.
Bishnupada Mukharji. Dated 7th May, 1943.
Mahammed Aynb Ali. Dated 15th May, 1943.
Vinayak Dattatraya Kirpekar. Dated 20th May, 1943.

Anath Nath De. Dated 25th May, 1943.
Puliyur Krishnaswami Duraiswami. Dated 25th May, 1943.

Vasant Ramdas Koppikar. Dated 29th May, 1943.
4th June, 1943

Gaurishankar Guha. Jagadish Narain Sinha.
Dattaram Laxuman Godambe.

Gurijala Pattabhi Ramayya. Dated 6th June, 1943.
Ramchandra Chintaman Shrikhande. Dated 7th June, 1943.

Om Prakash Verma. Dated 7th June, 1943.
Harendra Nath Dey. Dated 7th June, 1943.
Balraj Singh. Dated 8th June, 1943.

Lieutenant (Acting Major) Hari Prakash Lal is appointed Officer Commanding, Civil Defence Department, Government of India, Hospital Train No. 1, with effect from the afternoon of the 2nd July, 1943.

The services of Lieutenant L. E. Wharton are placed at the disposal of the Department of Education, Health and Lands, for employment as Deputy Assistant Director-General, Indian Medical Service (Recruitment), in the office of the Director-General, Indian Medical Service, with effect from the 1st November, 1942.

To be Lieutenants

Vellore Veraswamy Mudaliar Srienivasa Mudali.
Dated 9th January, 1943.

Eric Raymond White. Dated 6th February, 1943.

Donald Wilfred Shillong. Dated 7th March, 1943.

Chandra Mohan Dave. Dated 27th March, 1943.

Aylmer Joseph Nicholas. Dated 6th April, 1943.

Gerald Aloysius Burby. Dated 7th April, 1943.

Eugene Leopold Cyril Pnshong. Dated 7th April, 1943.

Eric Meneaud Wilson. Dated 9th April, 1943.

Nuggehalli Gopala Iyengar Govindaraj. Dated 9th May, 1943.

Domninus John William D'Costa. Dated 22nd May, 1943.

Jamshed Bakht. Dated 27th May, 1943.

Clarence Joseph D'Netto. Dated 30th May, 1943.

Krishna Kumar Bose. Dated 3rd June, 1943.

Pandarparambil Mathew Xavier. Dated 4th June, 1943.

Robert D'Souza. Dated 6th June, 1943.

Bankim Chandra Chatterjee. Dated 7th June, 1943.

Sheo Krishna Ray Chaudhuri. Dated 8th June, 1943.

Gopalakrishniah Natarajan. Dated 8th June, 1943.

Dudley James Toomey. Dated 12th March, 1943.

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CHOLERA:

ITS PREVENTION AND CURE

By A. J. H. DeMONTE, Diplomaed Bacteriologist
(Manch.), In-Charge, Bowel Disease, Research
Department, School of Tropical Medicine and
Hygiene, Calcutta.

With an Introduction by L. EVERARD NAPIER,
F.R.C.P. (Lond.), Editor of the *Indian Medical
Gazette.*

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Stanley Robert Edward Kitto. Dated 17th April, 1943.

Bajra Bhushan Bhadury. Dated 28th April, 1943.
Pagadala Radhakrishna Ramachandrudu. Dated 11th May, 1943.

Gouranga Lal Banerjee. Dated 15th May, 1943.
Terence Shanthakar Rao. Dated 11th June, 1943.

SECONDED TO INDIAN ARMY MEDICAL CORPS
(Emergency Commissions)
To be Lieutenants

Duncan Hector Robertson. Dated 19th January, 1943.

Vincent Aloysius Sales. Dated 28th February, 1943.
(Emergency Commissions)

To be Lieutenant

Donald Gordon Coutts. Dated 25th April, 1942.
To be Lieutenants (on probation)

16th January, 1943

Hannah Billig. Eunice Heath.
15th December, 1942

Emily Elspeth Grace Enid Gwenllian Fisher.
Baillie. Elizabeth Mary Morgan.

LAND FORCES—INDIAN MEDICAL SERVICE—SECONDED TO
INDIAN ARMY MEDICAL CORPS
(Emergency Commission)

(Women's Branch)

To be Captains

(Mrs.) Jean Robertson Biggar. Dated 20th April, 1943.

(Miss) Violet Mary Nazareth. Dated 10th May, 1943.

(Mrs.) Tharmapuram Krishnasami Sundaram. Dated 30th May, 1943.

(Miss) Nergesh Murzban Kothawala. Dated 8th June, 1943.

(Miss) Nivedita Sen. Dated 15th June, 1943.

(Miss) Perin Mullaferoze. Dated 27th May, 1943.

(Miss) Lakshmiraju Suryakantham. Dated 31st May, 1943.

To be Lieutenant

(Miss) Louisa Mary D'Silva. Dated 17th May, 1943.
(WITHIN INDIAN LIMITS)

To be Captains

Waman Daji Paude. Dated 2nd May, 1943.

Kadambi Krishnaswamy. Dated 7th May, 1943.

Mohammad Abdur Rahim Azhar. Dated 7th May, 1943.

Aiyam Rangaswami Anantaraman. Dated 4th June, 1943.

Sailendra Prosad Mitra. Dated 7th June, 1943.

(Women's Branch)—*To be Captains*

(Miss) Perin Ratnshah Edibam. Dated 14th April, 1943.

(Mrs.) Janaki Abdulkarim. Dated 14th May, 1943.

Moni Lal Paul. Dated 8th June, 1943.

To be Lieutenants

John Francis Bonjour. Dated 7th June, 1943.

(Miss) Dulcie Teresa Dias. Dated 31st March, 1943.

The undermentioned officer of the I.M.S. (E.C.) reverts from I.A.M.C. and is seconded for service in the Indian Air Force:—

Lieutenant B. P. Reddy. Dated 15th June, 1943.

INDIAN LAND FORCES
(Emergency Commission)

To be Lieutenant for service with Indian Air Force
Ramaswami Jayaram. Dated 16th March, 1943.

To be Lieutenant for service with Royal Indian Navy
Paul Frank D'Mellow. Dated 1st July, 1943.

PROMOTIONS

Lieutenant-Colonel to be Colonel

R. Hay, C.I.E. Dated 21st February, 1943.

INDIAN MEDICAL SERVICE—SECONDED TO INDIAN ARMY
MEDICAL CORPS

Majors to be Lieutenant-Colonels

8th July, 1943

G. P. F. Bowers. J. S. Riddle.
J. E. Gray.

INDIAN LAND FORCES

INDIAN MEDICAL SERVICE—SECONDED TO INDIAN ARMY
MEDICAL CORPS

(Emergency Commissions)

Captain to be Major

W. A. C. Nason. Dated 18th April, 1943.

Lieutenant to be Captain

A. E. Sundarean. Dated 25th January, 1943.

The undermentioned Captains are confirmed with effect from the dates specified.

LAND FORCES

INDIAN MEDICAL SERVICE—SECONDED TO INDIAN ARMY
MEDICAL CORPS

(Emergency Commissions)

P. A. L. Roberts. Dated 26th June, 1941.

M. B. Klein. Dated 10th July, 1941.

14th August, 1941

D. G. Horan. P. S. Clarke.

P. N. Swift. T. D. Brown.

W. Thomson. R. T. Hinde.

E. L. Jones. Dated 21st August, 1941.

27th September, 1941

W. N. O. George. D. S. M. Euraght-Mooney.

G. V. Faulkner. Dated 1st November, 1941.

8th November, 1941

T. H. S. Smith. W. M. Jones.

A. D. Dyson. D. A. Maclean.

P. Jacobs. F. A. Whittock.

29th November, 1941

J. E. M. Melville. H. R. S. Harley.

J. B. David.

20th December, 1941

O. Clarke. W. F. J. M. Thom.

D. MacAulay. G. E. Spear.

A. J. Sinclair. N. J. McQueen.

K. J. L. Scott. A. C. Mackenzie.

D. C. Logan.

10th January, 1942

R. M. Gilchrist. N. W. Gill.

E. D. Mackworth. P. H. Blackiston.

J. T. Miller. J. Cameron.

C. Sonick.

4th February, 1942

J. Mockler. M. A. Fawkes.

E. J. Currant. A. Maples.

H. Williams.

21st February, 1942

M. J. Barry. H. V. Knight.

J. A. W. Bingham. A. D. A. Maconochie.

G. R. Butterfield. J. W. Magner.

C. R. K. Carrol. J. M. Mungavin.

D. Currie. B. J. Niall.

H. M. Davies. G. L. L. Reynolds.

A. C. Greene. L. Rich.

F. A. H. Hall. J. L. Roberts.

R. C. Hallam. B. Rowlett.

G. Hannigan. C. G. R. Sell.

N. N. Iovetry-Tereshchenko. S. E. Vincent.

G. Barwell. Dated 14th March, 1942.

8th April, 1942

W. J. Aitken. T. Stephens.

A. J. M. Cathro. A. M. Merriweather.

C. H. Merry. W. M. Doolin.

W. E. Owens. J. D. Pibbs.

G. Quayle. T. E. W. R. Wood.

B. M. Medley. Dated 11th April, 1942.

A. A. M. Coutts. Dated 12th April, 1942.

4th May, 1942

A. Gray. J. S. Laurie.
D. Coutts.

7th May, 1942

H. M. Carlick. M. Lawton.
M. Scott. E. M. Eldrid.
J. T. Prendiville. Dated 16th May, 1942.

29th May, 1942

I. L. H. Hewlett. M. E. M. Blanden.
M. E. M. Flenning. I. D. Patterson.
D. A. K. Carnegie. Dated 6th June, 1942.

18th June, 1942

M. A. C. MacHugh. J. M. R. M. Johnson.
J. M. Durr-White. Dated 26th July, 1942.

29th September, 1942

N. K. Woll. G. M. Higgins.

INDIAN MEDICAL SERVICE—SECONDED TO INDIAN ARMY
MEDICAL COMPS

(Emergency Commission)

Lieutenant to be Captain

E. B. Weeks. Dated 17th August, 1942.

Lieutenants to be Captains

28th May, 1941

R. S. Saksena.	P. V. Ramaniah.
H. M. Kalapesi.	M. G. Nayar.
K. K. Jaswal.	N. I. Subrahmanyan.
W. G. Aranha.	N. G. S. Raghavan.
L. B. Belkhode.	D. D. Mitra.
M. R. Vachha.	K. P. Joseph.
A. A. Khan.	K. John.
H. L. Anand.	B. Raghavendrachar.
M. V. Sarma.	T. S. Ramanurti.
V. T. Kuriyan.	M. Ramarao.
B. L. Somway.	D. W. Khot.
M. S. Yehya.	A. K. Das.
M. A. Razak.	K. N. Jha.
K. B. Roy.	S. C. Bagchi.
S. G. Sundaram.	R. S. P. Sinha.
S. A. R. Iyengar.	K. G. Menon.
D. N. M. Rao.	G. V. Rao.
P. P. G. Tampi.	P. P. Kailasan.
K. M. R. M. Rowther.	K. P. M. B. U. Nayar.
P. R. M. R. Menon.	M. S. Sundaram.
C. W. Chacko.	K. N. K. Menon.
G. A. Alcem.	R. V. R. Rao.
L. Verghese.	J. Ramakrishna.
P. S. Viswanathan.	P. R. Raju.
B. A. Ranga Rao.	T. V. Ranganathan.

N. C. V. Raman.

M. Ayub Khan. Dated 13th June, 1941.
S. N. Mukerjee. Dated 15th June, 1941.
P. I. George. Dated 25th June, 1941.
T. Singh. Dated 2nd July, 1941.
P. S. D. Raj. Dated 10th July, 1941.
T. E. Unny. Dated 26th July, 1941.
P. S. Raghavan. Dated 17th August, 1941.
C. R. Mannadiar. Dated 26th August, 1941.
L. C. Wadhwa. Dated 1st September, 1941.
W. V. Bapiah. Dated 21st September, 1941.
V. K. Sundaram. Dated 17th October, 1941.
T. C. Verghese. Dated 28th October, 1941.
M. Mammen. Dated 2nd November, 1941.
R. E. Sinha. Dated 16th November, 1941.

PROMOTIONS

K. G. Raj. Dated 1st June, 1943.
A. Husain. Dated 2nd June, 1943.
P. B. Pandhy. Dated 4th June, 1943.
N. Sen. Dated 5th June, 1943.
A. Koka. Dated 6th June, 1943.

8th June, 1943

R. A. Mehta. G. S. Godiwalla.
R. C. S. Sandhu. Dated 9th June, 1943.
A. C. K. K. Raja. Dated 10th June, 1943.

12th June, 1943

P. Madhavan. R. N. Mitra.
D. Anjaneyulu. Dated 13th June, 1943.

15th June, 1943

P. F. Verghese. N. N. Das Gupta.

16th June, 1943

K. D. Ganguly. P. N. K. Menon.

18th June, 1943

L. D. Kale. R. Prasad.
V. A. Damodaram. Dated 19th June, 1943.
S. S. Bisht. Dated 21st June, 1943.

30th June, 1943

H. S. Saksena. M. R. Gagannathan.
M. Swaminathan.

SECONDED FOR SERVICE IN THE INDIAN AIR FORCE
(Emergency Commissions)

Lieutenants to be Captains

A. K. Basu. Dated 8th May, 1943.
B. K. Mukherjee. Dated 13th May, 1943.

RETIREMENTS

Colonel R. Sweet, M.S.O., K.N.P. Dated 7th July, 1943.
Colonel P. B. Bhattacha, M.B.E., M.S.O. Dated 21st
February, 1943.
Lieutenant-Colonel Jamal-ud-Din. Dated 30th April,
1943.

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Articles

THE TUBERCULOSIS CAMPAIGN IN INDIA : WHERE MUST THE EMPHASIS BE PLACED ?

By P. V. BENJAMIN, M.B., B.S., T.D.D.

Medical Superintendent, Union Mission Tuberculosis Sanatorium, Arogyavaram, near Madanapalle

THE tuberculosis campaign has been launched in India, but it is still rather like a frail bark on an uncharted sea. Since Her Excellency Lady Linlithgow issued her appeal at the beginning of the campaign, there has been a growing interest in the fight against tuberculosis, and in many different parts of the country, organizations and associations have been formed, clinics, sanatoria and hospitals have been established, surveys have been carried out, conferences have been held, and publicity has been given in the press. But it may be asked how much of this widely scattered anti-tuberculosis activity in the various areas is being conducted as part of a well-thought-out plan, and how much it will contribute to the ultimate control and decline of tuberculosis. There are places in which it would seem as if the starting of isolated bits of tuberculosis work, such as a clinic, was considered all that was needed for control of tuberculosis in those areas. It is now time for tuberculosis workers in India to visualize at what they are aiming in their various provinces, states and towns, and to plan a scheme which can be worked out in stages over a period of years.

In this paper I shall discuss the plan of campaign from three points of view only, namely the place of surveys, of clinics, and of hospitals and sanatoria in the control of tuberculous disease in the community.

The place of surveys in tuberculosis control

Enough work has by now been done in India to show that tuberculous infection is widespread, specially in the towns, and the time has passed for spending money and energy in doing tuberculosis surveys merely for the sake of finding out the incidence of tuberculous infection, except possibly in certain isolated groups of people. The vital statistics of towns, incomplete and inaccurate though they may often be at least as regards causes of death, afford plenty of evidence of tuberculous mortality and therefore morbidity.

The object of surveys should now be the detection of open and active tuberculous cases which are the sources of new infection, but such detection is of little use from the point of view of tuberculosis control unless, when the survey is being planned, some sort of provision is made for dealing with the cases so discovered. This means that surveys must be associated with an institution or organization which can deal with those needing treatment, and which can provide

treatment and can take measures to prevent spread of infection from the open cases. A further point of importance is that the co-operation of the public which is necessary for a tuberculosis campaign will not be forthcoming, or if it has existed will dwindle away, if nothing is done to meet problems brought out by the survey, especially the care of patients discovered and the prevention of spread of infection.

The place of the clinic in tuberculosis control

The most common tuberculosis institution in India at the present time is the clinic, and the Tuberculosis Association of India has rightly placed an emphasis on the clinic as the starting point of the campaign. But unless the true functions of a clinic are realized and its objects fulfilled, the clinic is of little use from the point of view of control of tuberculosis.

At the present time, most clinics are under the direction of the medical department of various provinces and states, and are staffed by doctors who are in general primarily occupied in diagnosis and treatment, and the public health aspect is overshadowed by the clinical aspect. There are various reasons for this. Most of the doctors in charge of clinics have had little training in public health work as compared with clinical training, and so naturally tend to spend more time on diagnosis and treatment with which they are more familiar. Moreover, it is well known that far more doctors are interested in clinical rather than preventive medicine. Many clinics are staffed by honorary or inadequately paid doctors who are forced to supplement their income by private practice, and public health work brings no fees. The staff, often too small even to deal with the large number of cases coming to a clinic, has little or no time for any activities outside the clinic. Moreover, the area and the population which most present clinics have to serve are far too large for a single clinic to be able to cope with as regards prevention of disease.

No clinic is exercising its primary function unless it includes within its work a preventive programme. The clinical side of the work should be confined mainly to diagnostic service, and treatment of patients diagnosed as tuberculous should be left to a different staff. At the present time it may not be possible to separate the two, but every clinic should plan to have this separation at the earliest possible moment. Tuberculosis officers in charge of clinics should have a public health training in addition to special tuberculosis training; this is insisted on in some countries in the West. A public health officer is not allowed private practice, and the salary is fixed after taking this into consideration. A tuberculosis officer should be on full-time work, should have the status of a health officer, should be debarred from private practice and should be paid adequately to compensate for this. Since one of the main functions of the clinic is prevention of the spread of the disease,

and since in carrying out this function, the work enters the domain of the public health department, there should be co-operation and co-ordination between the clinic and the public health department. It is a matter for consideration whether clinics should not come under the public health department altogether.

If, under present conditions, treatment has to be carried out in a tuberculosis clinic, there must be a staff large enough to ensure that the public health side of the clinic's work is not relegated to the background or swamped altogether. There must also be some limitation of the population which the clinic has to serve. For example, one clinic in Madras City with a population of over 700,000, cannot do the public health work which a clinic ought to do. If we really wish to tackle the tuberculosis problem, we should probably be planning for about 14 clinics for a population of 700,000, or one to about 50,000 people.

The published tuberculosis death-rate for a city such as Madras is about 200 per 100,000, and this admittedly is probably an underestimate. But assuming that it is true, it would mean 100 deaths a year in a population of 50,000 people, or if the usual calculation of the proportion of active cases of tuberculosis to deaths from tuberculosis is accepted, it would mean between 500 and 700 patients continually under the supervision of the clinic. Besides the patients themselves needing care and after-care, the families and contacts of the patients would also have to be closely supervised.

These ideas are substantiated by the figures (4th Annual Report, 1942) published by the Tuberculosis Association of India in connection with the work of the New Delhi Tuberculosis Clinic. In 1942 that clinic had to deal with 2,239 new cases of which 1,062 were found to be tuberculous, in addition to 355 tuberculous cases carried over from the previous year. There were 41,378 visits of patients for treatment and advice. During the year 745 new homes were visited by members of the clinic's staff, and a total of 4,716 house visits were made; 1,359 contacts were examined of whom 146 (10.8 per cent) were found to be suffering from tuberculosis. In two wards of the city, organized home treatment was arranged for 364 tuberculous patients. These figures deal with two items only of the clinic's work, namely its diagnostic work and a part of its preventive work, but they are enough to show the amount of work which a clinic will be required to do.

With the clinic, as with the survey, it is of no use diagnosing tuberculous cases unless some provision is made for treatment, and it is one of the functions of the clinic to arrange for that treatment. For some of the earliest cases of tuberculosis, general supervision and advice is all that will be necessary, and many of these can be looked after in their homes. But, taking again the New Delhi Clinic figures for 1942, we find that of 819 cases of pulmonary tuberculosis diagnosed during the year, 226 needed care in

an advanced disease hospital, 238 required prolonged and 277 short periods of institutional care, and only 78 did not need institutional treatment. This means that 741 patients needing institutional treatment had to be provided for, and it is known, although not stated in the report, that it was possible to find institutional treatment for only a very few of these.

The Tuberculosis Association has suggested organized home treatment as a solution for this problem, and the New Delhi Clinic is one of the very few places in India which is making a systematic attempt at this. In 1942, organized home treatment was arranged in two wards of the city for 364 patients, of whom 248 were pulmonary cases. But the experience of the clinic is 'that in a good percentage of cases, isolation was not at all possible in the homes'. From the point of view of the spread of tuberculosis, organized home treatment is only successful if the home conditions are such that isolation is possible. This leads us back again to the conclusion that the clinic cannot do its work from the point of view of tuberculosis control unless sputum positive cases can be provided institutional treatment, so preventing their infecting others.

Place of hospitals and sanatoria in tuberculosis control

It is well recognized all over the world by those who have studied the problem that one of the important contributory factors for lowering the death-rate from tuberculosis is the number of beds available for the treatment and isolation of tuberculous patients. The number of beds needed for tuberculous patients in a community has been studied in Western countries. A report on Tuberculosis Sanatorium Planning published in 1939 by the National Tuberculosis Association of America, states as follows:—

'The first step in planning either for a new sanatorium or for the enlargement of an existing one is to determine the number of beds required to meet the needs of the population group to be served. Experience has shown that when accurate vital statistics are available, it may be conservatively estimated that two beds should be provided for each recorded annual death. In communities where case-finding agencies are active and the sanatorium has a public appeal, beds in the proportion of three per death may be kept filled. When vital statistics are unreliable, an approximate estimate of the bed requirements may be made on the ratio of one bed per thousand population.'

These calculations are based on the American morbidity rates and for American general living conditions. In other countries where there is organized anti-tuberculosis work which has proved successful, the ratio between annual tuberculosis deaths and beds for tuberculous patients varies from 1:1 to 1:3; in Great Britain it is about 1:1, in Denmark about 1:2 and in Sweden 1:1.7. As far as our investigations show, the morbidity rates in India particularly in urban and industrial areas are much higher than in U.S.A. and the other

countries mentioned, and it is well known that living conditions are far inferior; therefore the ratio of beds to population and mortality should be higher if an effective campaign is to be carried out.

The lowest estimate for a town of 50,000 people in India according to the minimum standard of one bed to one death, assuming a tuberculosis death-rate of 200 to 100,000, would be 100 beds, or about 1,400 beds for a city the size of Madras. At present in the whole of the Madras Presidency with over 40,000,000 population, there are only just over 1,000 beds for tuberculous patients, including beds in tuberculosis institutions, general hospitals and jail hospitals.

What can be done in a city by a concerted effort against the disease is well demonstrated in the city of Detroit, U.S.A., which in 15 years reduced its annual tuberculosis death-rate from 1,300 to 680, or from 95 per 100,000 to 40.8 per 100,000, well below the national rate. The main method by which this reduction was accomplished was by the provision of about 3,000 beds for tuberculous patients, associated with the searching out the sick and treating them.

The mere starting of clinics without provision for isolation and treatment of patients discovered will never help to make any material headway against the disease.

Further, provision for treatment must be within easy reach of patients. There is an idea that sanatoria and tuberculosis hospitals should usually be built in what are thought to be specially favourable climates such as in the hills or in exceptionally dry climates. Climate has some place in the treatment, but it is comparatively small; what matters most is the treatment itself, and this can be given anywhere provided that there is a properly trained staff and necessary equipment. The need that now faces all major Indian towns is the building of tuberculosis hospitals within easy reach of the population, to begin with one bed per 1,000 population, increasing to one bed per tuberculosis death and then to the more ideal standard of two beds to each tuberculosis death.

This programme will be a costly programme, but nothing less will have any real influence on the tuberculosis death-rate. Much of the tuberculosis work in India hitherto has been a mere tinkering with the problem and with little real effect as regards control of the disease. With a tuberculosis problem so vast as that in India, it is impossible to begin with a full scheme all at once to be introduced in three or four years, and beginnings will have to be small, but these small beginnings must be part of a thought-out scheme for each area, to be introduced and developed as rapidly as possible, until every tuberculous patient is able to get the treatment he needs, not just for his own sake, but for the sake of preventing his being a source of infection to others. When we shall have reached this stage, and then only, we shall have made real headway in controlling tuberculosis in India.

THE OPEN CASE IN RELATION TO THE CONTROL OF TUBERCULOSIS

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THE modern concept of the spread of tuberculosis from an open case to a susceptible person dates back to pre-Koch times. Hippocrates, Sylvius and others recognized the infectious nature of tuberculosis long before Koch discovered the tubercle bacillus, but their understanding of the nature of infection was at best vague. Koch's discovery gave point to the infectious nature of the disease.

In his second publication dealing with the tubercle bacillus, issued in 1884, Professor Koch made a prophetic statement that it would take a generation or more for students to realize the possibilities and implications of his discovery. The truth of his statement is borne out by the slow growth of scientific knowledge as to the means of spread of infection. It has taken years to bring to complete realization the truth that the infecting germ passes from one living organism to another, either directly or indirectly, whether the contact is personal or the infecting material is ingested or inhaled.

It is understood that our discussion of the importance of the open case represents but one part, albeit the most important part, of the field of infection. In countries where raw milk is an important part of the diet, and where the milk-producing animals are not carefully supervised, the importance of the bovine type of tubercle bacillus must in no way be minimized. However, in countries where cattle are frequently tested for tuberculosis, or, where milk before using is boiled or thoroughly pasteurized, bovine infection seems to be of much less importance than the human infection.

For the purpose of this paper it is useless to debate the question as to whether a tuberculous lesion in a human being is developed from bacilli implanted at any age, or from an infection contracted early in life and developed later. Since we are considering infection in general, and since it is generally admitted that, except for very exceptional cases, all human offspring are born free from infection, all implantations must be extra-uterine and, therefore, primarily exogenous. Moreover, modern studies show that in addition to possible infection early in life which may provide a partial immunization, massive exogenous infection in later years must in the majority of cases be held responsible for active disease.

Early studies of this subject have been made by English, French, German and American workers. In these countries the importance of the sputum-positive case has been recognized from the early years of the present century. It is true that the first institutions for advanced

cases of tuberculosis were founded more from the humanitarian duty of caring for the sick poor than from the idea of preventing infection. For the last thirty-five years, however, that is since the presentation by Sir Arthur Newsholme (1908) at the Sixth International Congress in Washington, D.C., of the study of the causes of the decline in the tuberculosis death-rate and his emphasis on the value of segregation, the isolation of the open case has been a powerful argument to promote the establishment of hospitals and sanatoria. But the scientific basis for this belief in the importance of the sputum-positive case has received intensive study only during the past few years. For this recent development, the new technique of case finding and of diagnosis through the tuberculin test and the x-ray is no doubt largely responsible.

From the date of the publication of the von Pirquet test in 1907, studies of the number of cases of infection, especially among children, were made in great numbers throughout the civilized world. In many of these studies, however, the distinction between the children exposed to the open case and those with no known history of exposure was not marked.

In 1923 Lampson published some remarkable figures from tests made of families in a rural area. Of those exposed to open tuberculosis, 67 per cent gave a positive reaction; those exposed to arrested tuberculosis gave 33 per cent positive reaction; to latent tuberculosis, 22 per cent; and of those where no known exposure was found, only 2.5 per cent gave a positive reaction. His investigation showed that the intimacy and length of exposure are the determining factors in infection.

In 1924 Slater published the results of a tuberculosis survey in a rural community in which the incidence of infection was very low. In his study of 1,654 school children, he found 80 per cent positive among those who were known to be in contact with an open case, while only 5 per cent were positive where there was no history of exposure.

In 1925 Myers and his associates published an extensive study of 2,000 pupils in the Lymanhurst School. He found 57 per cent positive among those with definite exposure to an open case, 38 per cent positive where the exposure was doubtful, and 28 per cent positive where there was no history of exposure.

In 1942 Mark conducted a survey in seven rural countries. The survey included Mantoux testing of school children and adults and x-ray filming of reactors. In all, 20,720 persons were tested. A total of 2,939 persons reacted, of whom 1,312 gave a history of family exposure. In this 'intimately exposed' group, 7.1 per cent were found to have active tuberculosis. In the 'casually exposed' group of 1,627 reactors, the yield of active cases was only 1.0 per cent.

Brailey (1940), in a very illuminating study, demonstrated that familial contact with sputum-positive cases carries a risk of infection twice

as great as similar association with sputum-negative cases. Her study was limited to households in which there was or had been a definitely diagnosed case of pulmonary tuberculosis in an adult.

In the series of studies on tuberculosis by Opie, McPhedran and Putnam published in 1935, based on an investigation of 1,000 families of 5,117 individuals from the out-patients' clinic of the Henry Phipps Institute, Philadelphia, whose records continue over a maximum period of eight years, the results are most interesting.

For the purpose of this article the conclusions drawn in the second paper of the series are given in the words of the authors:—

'The spread of tuberculosis occurs in large part by long drawn-out family or household epidemics in which the disease is slowly transmitted from one generation to the next.

The tuberculin test which is a fairly accurate index of existing tuberculous infection, shows that a large part (71.6 to 79.3 per cent) of children of households in contact with persons with tubercle bacilli in the sputum have acquired infection within the first five years of life.

In household in contact with a member with tuberculosis but with no discovered tubercle bacilli in the sputum, the number infected is relatively small (28.7 to 30.9 per cent) in the first five years of life; and throughout childhood, adolescence, and early adult life it is only slightly greater (about 10 per cent more) than in persons with no contact with the disease.

Roentgenographic examination, which reveals the anatomical position and extent and in some degree the character of tuberculous lesions of the lungs, shows that discoverable lesions appear in a large part in the young children exposed to open tuberculosis (39.9 per cent of children between 0 to 4 years) and infrequently in young children of families exposed to tuberculosis with no discoverable tubercle bacilli in the sputum (1.2 per cent of children between 0 to 4 years). Throughout the remainder of childhood and adolescence the incidence of lesions with exposure to open tuberculosis far exceeds that with contact with tuberculosis but with no demonstrable dissemination of tubercle bacilli.

Approximately one-third of children exposed to open tuberculosis acquire calcified nodules of lungs or lymph nodes recognizable during life. The incidence of these lesions is far less in children exposed to tuberculosis with no known dissemination of tubercle bacilli and still less, though still considerable, in children with no known exposure to tuberculosis.

Infiltrating lesions of first infection or childhood type (latent and clinically manifest) are numerous (17.4 per cent) in children from birth up to five years of age exposed to open tuberculosis, but are not found in children of the same age exposed to tuberculosis but with no dissemination of tubercle bacilli. Later, they become numerous in both groups but disappear in early adult life. In children after 15 years of age, infiltrating lesions with no symptoms or physical signs (latent infiltrating lesions of first infection) are "strand-like" and evidently healed or in process of healing.

Lesions of adult or re-infection type first appear in the age period of 10 to 14 years, and before the age of 30 years are more frequent in members of families exposed to open tuberculosis than in families where tuberculosis exists, but with no recognized tubercle bacilli in the sputum. At a later period of life, manifest disease of re-infection type is found more frequently in members of families with tuberculosis with no known dissemination of tubercle bacilli, doubtless because in these families it pursues a more chronic course.

In persons who have been in contact with tuberculosis and react to tuberculin, the incidence of lesions demon-

strable by roentgenographic examination increases with increasing sensitivity to tuberculin, being least (13.3 to 17.0 per cent) in those who react to 1 mg., more (41.5 to 46.9 per cent) in those who react to 0.1 mg., and highest (50.8 to 68.7 per cent) in those who react to 0.01 mg.

In the foregoing studies, the importance of the family as the centre of infection in the spread of tuberculosis has been strongly emphasized. When investigating the spread of infection, however, we must not assume that the open case is of importance only in the family. This point has been demonstrated in the study by Downes (1936). Intensive study was made of 83 families with 105 new active cases. Of the 105 active cases, only 34 per cent showed familial contact and approximately 66 per cent represented the proportion of active cases in which the source of infection was outside the family. Yet, after careful consideration of the 334 contacts in the 83 families, the author concludes that 'the risk of contracting serious tuberculosis was 13 times greater for all family contacts than for persons in the community at large'. She adds that 'extra-familial contact is undoubtedly a more important factor in the spread of tuberculosis in a rural area than has been generally believed'.

It is evident from these investigations that the frequency of infection and disease in any age group varies directly with the degree and length of exposure to open tuberculosis. Persons living in close contact with an open case, such as is associated with the intimacies of family life, run a significantly greater risk than those who are exposed casually, that is, outside of the home, exposure usually being to an unknown source.

These well-controlled studies have brought home to us the far-reaching significance of Koch's discovery. That tuberculosis breeds tuberculosis is now recognized with all its implications as the basic principle of the epidemiology of tuberculosis. The infectious nature of the disease is to the fore. Elimination of open tuberculosis from the community will mean eradication of the disease. Where there is no seed, there can be no harvest, regardless of the type of soil.

What method then is practicable to eradicate this age-old scourge of mankind?

Case finding and isolation

The first step of prime importance that suggests itself is to isolate all patients with positive sputum under conditions wherein they cannot endanger others. Obviously such a programme must include not only the infectious cases but also finding those in the early stages of the disease.

Since the first mass case-finding programmes were conducted among school children, it may well be to say a few words about these. Recently, through experience, it has been realized that school surveys are not a fruitful means of case finding. Children of school age

have very little re-infection tuberculosis and almost never have it in a communicable state.

A review of recent studies among school children reported by sixteen investigators (quoted by Mark, 1942) reveals that among a total of about 635,000 school children of all ages, including some in colleges, the percentage of yield of active cases varied from 0.8 to 1.6 per cent. The latter percentage was found in college students.

Observations made by Edwards (1940) and Godfrey (1941) led them to the conclusion that case finding in school children was expensive and comparatively unproductive. Godfrey goes so far as to say that the 'promiscuous tuberculin-testing of school children is a waste of time, money and effort'. The cost of finding a re-infection case of tuberculosis among school children was found by Pleyte *et al.* (1937) to be 1,400 dollars and by Zacks (1931) 1,430 dollars. In reporting the experience of New York State Tuberculosis Clinics, Plunkett states (quoted by the writer, 1940) that because of the large number of persons that must be examined to find a case, it costs over 4,000 dollars a case to find tuberculosis in the age group from 0 to 14, whereas from 15 to 24 it costs only 187 dollars and grows less with each decade until after 45 years it only costs 77 dollars per case.

In regard to case finding in special population groups, Edwards (1940) has shown that, when special groups are carefully chosen, a sufficient number of cases will be found to make such studies of value. In recommending special groups for investigation, consideration has to be given to the social and environmental conditions as well as to the morbidity and mortality records of the community.

Webster (1941) and Mark (1942) conducted a survey in a rural country of some 50,000 population. The survey included examination of all members of families in which there was or had been a case of tuberculosis. The cost of finding a new re-infection type case of tuberculosis, whether active or inactive, was 96 dollars. If only active cases are considered, the cost was 159 dollars. Compare these figures with those reported by Pleyte, Zacks and Plunkett, given above.

From a biological point of view, it is not necessary to find every case of tuberculosis and isolate him. Reduction of the number of cases in a community to a minimum will, in time, through natural processes be sufficient to bring about the desired results. Frost (1937) found through statistical analysis of available epidemiological data that 'it is only necessary that the rate of transmission be held permanently below the level at which a given number of infection-spreading cases succeed in establishing an equivalent number to carry on the succession'. This is known as 'biological balance'. Godfrey (1941), in a recent article, has emphasized the same idea.

Collapse therapy

Another plan which is entirely practicable is to endeavour to close the cavities that are the sources of the bacilli in sputum. Whether this is done by prolonged bodily rest or by surgical interference, the result is the same, *viz.*, sealing of the foci of infection. Surgical procedures to effect the closure of cavities are of increasing importance. Pneumothorax, pneumonolysis, oleothorax, phrenic neurectomy, plumbage and thoracoplasty are directed towards the putting of the diseased lung at rest, the closing of cavities and the changing of an open case into a closed one. The results are often dramatic. By their means the spread of infection is cut down, and hospitals are able to register a quick turn-over of cases.

Education

A third practicable plan is the education of the open case as to the precautions necessary for the protection of others. The educational programme must include the education of the patient's family and associates if we are to control the spread of tuberculosis from the open case.

To sum up: The modern campaign against tuberculosis, to quote Loing (1935), 'centres around the patient with open tuberculosis expectorating bacilli. Reduced to its simplest terms the object must be to find the open case, and bar it as a source of contagion to others'.

Summary

1. With the discovery of tubercle bacillus the communicable nature of the disease was established, but it has taken almost a generation to realize the possibilities and implications of this discovery.

2. Well-controlled studies by many workers indicate that the best procedure to follow for the eradication of the disease, is the isolation of the infectious case and the examination of all intimately exposed persons.

3. The programme for tuberculosis control must include finding not only the open cases, but also cases in early and non-infectious stages of the disease.

4. The frequency of infection and disease in any age group in a community varies directly with the degree and length of exposure to open tuberculosis.

5. School surveys are expensive and are not a fruitful means of case finding. Studies of special population groups are more productive of results.

6. The spread of tuberculosis occurs in large part by long drawn-out family or household epidemics in which the disease is slowly transmitted from one generation to the next.

7. In view of the communicability of the disease the practicable programme of control that suggests itself is:

(a) Isolation of open cases.

(Concluded at foot of next column)

WAR AND TUBERCULOSIS

By T. J. JOSEPH, B.A., M.B., B.S. (Madras),
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WAR and pestilence have always been associated. In fact, until recent times, sickness nearly always surpassed battle wounds as a cause of mortality in contending armies. For hundreds of years, waves of typhus fever, plague, cholera, small-pox, dysentery, and typhoid fever have broken out in warring nations, decimated armies, and spread malignantly through the populations of opposing lands. 'Rats have killed more human beings than all the wars since Christ.'

Naturally these acute epidemic diseases which killed large numbers in dramatically short periods of time attracted most attention, and effective measures were taken against them. Civilian as well as army records of health during this present war show that these large scale epidemics of acute diseases have been conquered to a large extent by improved public health measures and more efficient army medical services.

As long as mortality due to these acute epidemics remained overwhelming, the rise in mortality due to tuberculosis during war was not

(Continued from previous column)

(b) Closure of cavities.

(c) Education of the patient and his associates.

8. Collapse therapy is to be looked upon not only as an individual therapeutic measure, but as a public health procedure of great significance.

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evident. However, as the acute epidemics became more and more controlled, and as the means of exact diagnosis of tuberculosis and the machinery for collecting reliable tuberculosis statistics became more and more perfected, the increase in the menace of tuberculosis both in military services and in civil populations during war became more and more apparent.

Tuberculosis and the world war of 1914-18

There is reason to believe that long wars accompanied by privation have always led to increase in tuberculosis. The siege of Paris in 1870-71 quadrupled the general mortality in six months. In the augmented number of deaths, a large increase in tuberculosis was noted. It is said that even the character of tuberculosis changed from chronic to acute form. But it was the world conflict of 1914-18 that revealed tuberculosis for the first time as a major war problem. One of the things that drew pointed attention to this problem was the discovery of large numbers of tuberculous troops in the French army. The French medical military service returned 86,000 soldiers to civil life with a diagnosis of acute tuberculosis within 5 months of the outbreak of war, and by February 1917, the reported number had risen to 150,000. Exchanged prisoners of war afflicted with tuberculosis were also returning to France by thousands.

This report spread alarm throughout Europe and even to the U.S.A.; so much so, that an eminent public health official, Hermann M. Biggs, was sent to France in 1917 by the International Health Board of the Rockefeller Foundation to study the situation on the spot. Terrible examples of fatal rise in phthisis were discovered in beleaguered and conquered cities such as Warsaw and Belgrade where tuberculosis took on almost an epidemic form. The tuberculosis mortality in Warsaw increased from 320 per 100,000 before the war to 975 in 1917, accounting for a quarter of all deaths. In Belgrade, tuberculosis mortality reached the appalling figure of 1,483 per 100,000 of the population in 1917. Three hundred and eighty cities of more than 15,000 population in Germany showed an increase from an average mortality of 157 per 100,000 in 1913 to 287 in 1918. All over Europe an increase varying from 10 per cent in favoured regions to more than 200 per cent in the most seriously affected was noted, with persistence of the rise for 2 to 5 years. Esmond R. Long states:—'It would probably be conservative to estimate a rise of 15 per cent in tuberculosis mortality for 3 years in all Europe, which would credit the war with about 200,000 tuberculosis deaths.

Lessons from the war of 1914-18

During the post-war years, much labour was spent in assembling mortality records of the war years in the civil populations of all the countries engaged. It was evident that tuberculosis was exacting a great toll, unrecognized in the wars of previous years. Three graphs showing the trend of tuberculosis mortality in England and Wales, Northern Ireland and Italy are given here.

These countries were not chosen because they were the most directly affected by the war, but merely because these graphs are available to the writer. Corresponding graphs for countries more directly affected by the war, France, Germany, Poland, Austria, etc., would probably show an even more marked rise of the mortality curve during the war years.

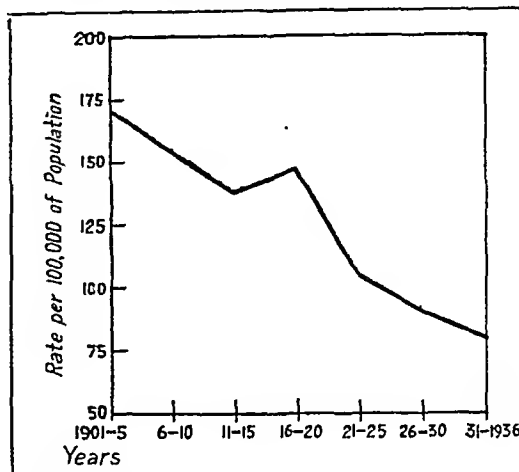
The explanation of the increase in tuberculosis in Europe during the first world war has been the subject of much research. Wolff called the war

an 'involuntary mass experiment of more epidemiological significance than endless theorizing on the pathology of tuberculosis'. Crowding, malnutrition, exposure, overstrain, etc., have all been thought responsible in varying degrees by different students.

GRAPH 1

England and Wales.

Death-rate from tuberculosis at all ages.
1901 to 1936.

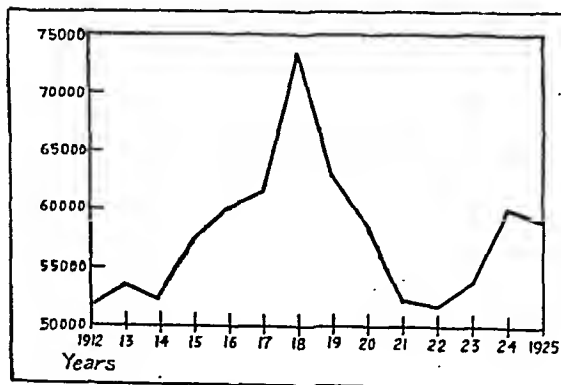


Those who held the view that malnutrition was the chief debilitating factor which reduced resistance and opened the door to infection, pointed out that in Germany the adult dietary intake sank from a daily average of 3,000 calories with 12 per cent protein, 20 per cent fat and 68 per cent carbohydrate before the war to 1,400 calories with 8 per cent protein, 9 per cent fat and 83 per cent carbohydrate at the end of the conflict. In 1930, twelve years after the close of the war, years characterized by a phenomenal growth in

GRAPH 2

Italy.

Total tuberculosis mortality.
1912 to 1925.



the science of nutrition, Schroeder reviewed the German epidemic of tuberculosis. His analysis convinced him that the nutritional factor was the basis for the tuberculosis rise, and that insufficiency of protein was chiefly responsible. His observations indicated that, when the protein level was reduced below 80 grammes per day,

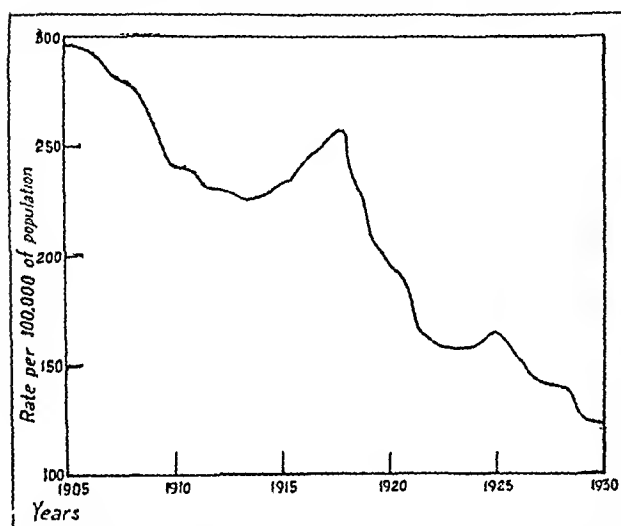
the good progress of tuberculous patients in hospitals ceased. The effect of protein was, in his opinion, due to its specific dynamic action. He held that a high metabolic level was important in resistance to tuberculosis.

Those who laid emphasis on overstrain as the cause of the rise in tuberculosis mortality, pointed out that in France and England, the chief rise in tuberculosis rates was in young women, and since neither country suffered seriously from under-nourishment and both called heavily upon young women for industrial service, the increase was attributable to the strain of increased labour.

GRAPH 3

Northern Ireland.

Death-rate from tuberculosis for each year from 1905 to 1930.



Various authors referred to a change in type of tuberculosis, as war conditions lasted, with a tendency to assume a more generalized form. Analysts with the widest experience warned against a narrow view and superficial acceptance of one or other of the several possible causes as solely responsible, and pointed out that the incidence of tuberculosis ran very close with any radical disturbance in a country's socio-economic structure.

Just as the rise in tuberculosis mortality in war times is rapid, the return of the mortality rate to the normal level after the restoration of peace and normal conditions is also rapid. Observers who held the view that the war of 1914-18 undid all the favourable effects of decades of previous public health work turned out to be too pessimistic. Rapid recovery took place in most countries within a few years.

It was observed that in most countries the proportionate rise in tuberculosis mortality was greater than the rise in general mortality.

A noted fact of considerable epidemiological interest was that during the years of recovery from the effects of war, the mortality curve in some countries tended to fall below the pre-war normal level. Many theories were put forward to explain this phenomenon. Probably the real

explanation is that many tuberculous patients, who under normal conditions would have died only later, died off earlier under the strain of war, leaving fewer tuberculous patients to die during the immediate post-war period.

A parallel is seen in the following example: In New York State in October 1918, tuberculosis mortality was 50 per cent higher than the expected rate for that month. It was at that very time that influenza was raging most violently in that state. It is quite likely that the excess tuberculosis deaths were mostly due to influenza in tuberculous patients. There was a notable drop in tuberculosis mortality during the following year. This was probably due to the fact that the influenza epidemic had carried off a large number of advanced tubercular patients who would have died of tuberculosis alone during 1919.

In countries such as Germany where the economic strain became worse during the post-war period, the tuberculosis mortality curve showed a secondary and more persistent rise during the later post-war periods.

Tuberculosis and recruiting

Before and during the war of 1914-18 much controversy went on among tuberculosis workers and among army medical authorities regarding the standards to be adopted in the examination of recruits with a view to excluding tuberculosis from the armies of different countries.

There was much divergence of opinion among experts regarding the advisability of admitting into the army persons with 'arrested' tuberculosis. H. M. Biggs, who was sent to France in 1917 by the International Health Board of the Rockefeller Foundation specially to study tuberculosis in the army, recommended that stringent examinations be made in order to exclude tuberculosis in recruits. He held that any man with even a very limited amount of pulmonary tuberculosis that is latent or arrested, is almost certain to break down under the strain of military training and army life. Others including Fishberg believed that military service was no more likely to activate dormant lesions than any civil occupation requiring muscular effort and that soldiers with arrested tuberculosis could stand war's hardships well. Extremists in this view even contended that exercise and change in climate were so beneficial that it was wise to send patients into the army for health! Admission of tuberculous patients into the army was facilitated by another opinion held by some experts in those days, namely that exogenous infection was extremely unlikely in civilized adults and that, therefore, the spread of tuberculosis in military camps was not to be feared.

Subsequent experience proved that those who held the view that persons with tuberculosis should be rigidly excluded from the army were in the right. Countries which made the early mistake of recruiting without proper chest examinations had reason to regret their mistake

later on. For example, the U.S.A. army authorities found out to their cost that the prevention of tuberculosis in the army is much cheaper than cure. The records of the 'Veteran's Administration' of the U.S.A. showed that, up to 1940, tuberculosis in veterans of the first world war cost the country 960,000,000 dollars in compensation, vocational training, insurance and hospitalization.

A patient who gains admission into the army and then gets invalided with a medical certificate of 'disease attributable to military service' stands to gain. Hence the saying 'It does not pay a recruit to be diagnosed too early'.

Soon after the U.S.A. joined the war, the National Tuberculosis Association of America appointed an advisory committee on the military problems of tuberculosis. This committee outlined a programme calling for recruiting examinations, re-examinations during service, and treatment of cases discovered. This committee also recommended that expert consultants be appointed throughout the country to consider the acceptance of prospective recruits referred by army physicians as suspected cases. Boards of expert examiners were accordingly set up to check the state of the lungs of every man admitted to the army. Regulations for the guidance of medical officers in examining for pulmonary tuberculosis were given in elaborate detail in order to ensure efficiency and uniformity of practice.

There was much dispute among experts regarding the comparative merits of physical examination and radiology in the diagnosis of tuberculosis. The army regulations by above-mentioned stressed physical examination by percussion and auscultation, decisive significance being given to moist râles heard on inspiration after cough. Now that radiology has acquired a predominant place in the diagnosis of tuberculosis, it seems strange that as late as 1918 American experts should have written: 'As compared with physical examination, roentgenological examination, even when done by an expert, occupies a place of secondary importance in the diagnosis of tuberculosis of clinical significance'.

When speed became a vital necessity for the rapid provision of man power, 50 examinations per day per physician were set as the standard for the examining boards. When x-ray examinations came to be more widely used, it was estimated that two staffs could make satisfactory examinations of 1,000 men a day at an expense of one dollar per man. The number of men actually rejected by tuberculosis examiners in the U.S.A. was 22,596 out of 3,288,669 persons examined, the discharge rate being 0.689 per cent.

Tuberculosis and the present war

The lessons of the war of 1914-18 were acted upon by many countries during the present war.

A rise in tuberculosis was expected and precautions were taken as far as possible. Attempts were made to exclude tuberculosis from armies. For example, in June 1941, the Adjutant-General of the U.S.A. army issued the following order: 'In view of the great importance of chest x-ray examinations in the exclusion of individuals with pulmonary tuberculosis and other significant intrathoracic defects from the military service, it is directed that provision be made without delay for the inclusion of chest x-rays in the examination of all registrants appearing before induction boards'. Standard size x-ray films, paper films, and 4 by 5-inch miniature films were extensively used. Men showing anything more than 'small fibroid lesions represented in roentgenograms as sharply demarcated strand-like or well-defined nodular shadows not exceeding a total of 5 sq. cm. in standard size films' were to be rejected. Calcified lesions barred men from acceptance only when they were large and multiple. The rejection rate for tuberculosis in the U.S.A. recruiting centres varied between 0.5 and 1.5 per cent.

The necessity for mass recruiting examinations is looked upon in the U.S.A. as a great opportunity for tuberculosis case-finding. Country and state public health services, tuberculosis societies, local boards, etc., are co-operating to look after those rejected for tuberculosis before acceptance into the army. The 'Veteran's Bureau' takes charge of those rejected after induction into the army. Experts have estimated that in 6 millions called up, 88,000 tuberculous cases will be discovered and that their care will cost the state about 42,000,000 dollars apart from pensions, etc.

Tuberculosis mortality figures of most countries for the present war years are not yet available. However in June 1941, the London correspondent of the American Medical Association referred to tuberculosis as the single exception in a satisfactory public health situation in England. The British Ministry of Health reported a rise of 9.7 per cent in the mortality from tuberculosis in 1939 and 1940, the increment being greatest in young women. The selective mortality in young women is strongly reminiscent of the last war. The tuberculosis mortality rate for London was 78 per 100,000 of the population in 1939 and 97 in 1940.

Modern war is total war. New factors favourable to the spread of tuberculosis have been created by the change in the nature of warfare. Some such factors are: greatly accelerated industry leading to crowded quarters in by mass migrations and evacuations which make it very difficult to distinguish or segregate the sick and the well, evacuation of tuberculosis institutions to make room for war and air-raid casualties, crowded air-raid shelters where tuberculous patients cannot be excluded, the

forced billeting of tuberculous cases on healthy households, black-out conditions preventing ventilation and favouring cross-infection, etc.

Food rationing and tuberculosis

In the light of the experience of Germany and other countries during the last world war, nutrition was under constant consideration in all countries as an essential preparation for the present war. Countries which had long prepared for war in view laid up huge stores of food materials and organized rationing of food even before the beginning of the war. However, malnutrition, which is acceptedly one of the foremost predisposing causes of tuberculosis, is evident in various countries, especially the occupied countries. In 1941, deficiency oedema had already appeared in some parts of Belgium in spite of a system of rationing. In Spain in 1941, the daily calorie average was only 800 to 900 for adults. In France the corresponding figure was 1,400 to 1,500. The International Health Division of the Rockefeller Foundation, after sample surveys in France in 1941, reported that moderate deficiency in vitamin-A concentration in the body was seen in all age groups. Vitamin-C deficiency was evident to a slight extent by physical examination, to a greater degree by blood studies, but not apparent by skeletal roentgenography. According to current newspaper reports, there is widespread famine in Greece and the Balkan countries. Whether these nutritional defects are accompanied by a corresponding rise in tuberculosis remains to be seen.

The U.S. National Research Council has recommended a daily intake of 2,500 to 3,000 calories for a man of 70 kg. weight, the variation being according to activity; 2,100 to 2,500 calories for a woman of 56 kg. The protein requirement for an active man is given as 70 gm. and for a woman 60 gm. Other standards laid down are: calcium 0.8 gm.; iron 12 mg.; vitamin A 5,000 international units and ascorbic acid 75 mgm.

The British Ministry of Health set up a Standing Advisory Committee on tuberculosis to overcome war-time difficulties of the tuberculous. This committee maintained close touch with the Ministry of Food concerning the question of rationing and tuberculosis. It was shown that with rationing as it was, it was possible to devise a diet that was qualitatively and quantitatively adequate and balanced and containing the necessary vitamins. War conditions in England have shown that the originality and initiative of kitchen staffs can overcome many problems which would have been considered insuperable in peace time. Institutions in England which have ample space are now growing vegetables in places previously reserved for flower beds, and the breeding of rabbits for meat is becoming a common practice. In some places food scraps left over by patients are collected and specially treated by heat and fed to livestock.

War and tuberculosis in India

The Indian army has recruited about 2 million men. How far medical examinations carried out before recruiting are effective in excluding tuberculosis from the army is not known. As mentioned above, the rejection rate for pulmonary tuberculosis in the U.S. army was between 0.5 and 1.5 per cent. The rate in India is certainly not likely to be lower. Making a very conservative estimate of a 1 per cent rejection rate in India, an adequate examination of the 2 million recruits would have detected about 20,000 tuberculous cases. If any large proportion of these men have been accepted in the army, most of them will in course of time be invalided and will need to be looked after.

Until recent years, sepoys invalided out of the Indian army on account of tuberculosis were mostly left to look after themselves. But it is a matter of gratification both to soldiers as well as the general public that the Indian army is now coming to recognize the menace of tuberculosis in the ranks. Hospital accommodation is being reserved for serving soldiers who have fallen victims to tuberculosis, in various places such as Deolali, Kirkee, Bikanir, etc. More permanent schemes are under contemplation.

The Tuberculosis Association of India have built a fine block of buildings for soldier patients at the Lady Linlithgow Sanatorium. The Defence Department of the Government of India met the major part of the cost of this building, and also pays a large annual grant for the maintenance of these patients. Men evacuated from Dunkirk, North Africa and Singapore are here fighting the tubercle bacillus with the same vigour and determination with which they fought the Germans and the Japanese. The Indian Red Cross is liberal in providing comforts and amenities for these patients. Members of the women's voluntary service have made a beginning in providing occupational and diversional therapy for these men. Soldier patients seem to be more amenable to this form of treatment than the average civil patient.

Figures are not available to show how the war of 1914-18 affected tuberculosis in India, nor do we know the effect of the present war. All that one can do at present is to draw inferences from figures from other countries. Therefore the writer offers no apology for having quoted figures extensively from other countries, especially the U.S.A. In this connection the writer also wishes to acknowledge that in the foregoing paragraphs verbatim extracts have been made from the article on 'War and Tuberculosis' by Esmond R. Long in the *American Review of Tuberculosis*, Vol. XLV, No. 6. This was considered worth while on account of the topical interest of the subject at the present time.

The average level of nutrition in India in times of peace and prosperity is probably lower than the level of war-time nutrition in Great

(Concluded on opposite page)

TUBERCULOSIS SURVEYS IN AN URBAN AND A RURAL AREA IN BENGAL*

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THE Indian Research Fund Association has published a report which was drawn up by the Tuberculosis Survey Sub-Committee for the

* Abridged from a report of the Bengal Public Health Department.

(Continued from previous page)

Britain or the U.S.A. There is no doubt that the war has brought this level still lower. It is safe to infer that the war will cause a great increase in the already high mortality and morbidity due to tuberculosis in India. Here is a cause worthy of the attention of administrators, philanthropists, legislators, local bodies, members of the medical profession and the public in general who are aware of the enormous problems of post-war reconstruction confronting them. Luckily for India, a national association for the prevention and control of tuberculosis, namely the Tuberculosis Association of India, has been brought into being at the right moment of the greatest need. It is hoped that this association will grow in strength and play a worthy part in the fight against tuberculosis in post-war India.

Summary

1. The effect of war conditions on tuberculosis incidence is described, and the causes for the increase in tuberculosis during war times are discussed.
2. Tuberculosis problems in relation to recruiting for the army are discussed.
3. The effect of war-time food restrictions on tuberculosis is discussed.
4. The place of anti-tuberculosis work in post-war reconstruction in India is pointed out.

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technical guidance of those engaged in carrying out tuberculosis surveys in different parts of the country. They have standardized the methods of observation, analysis and presentation of results of two types of surveys. Type I survey is conducted with the object of ascertaining the incidence of infection and type II survey for finding out morbidity rate and clinical types of the disease in a community and in its different sections.

The present communication is a practical application of the procedure suggested by the sub-committee, to two areas in Bengal, viz, Serampore, a small town near Calcutta, and a rural community in Barisal District. Since these are perhaps the first set of surveys carried out along these lines, it is hoped that they will be of some help to those engaged in similar studies in other parts of the country. At any rate, results presented here, which we believe throw some light on the tuberculosis problems of this province, will be of use, for purposes of comparison, to those interested in tuberculosis problems elsewhere. It may, however, be mentioned that for various reasons it became necessary to combine types I and II surveys in one study; this is a departure from the recommendations of the sub-committee which recommends that type I survey should precede type II survey.

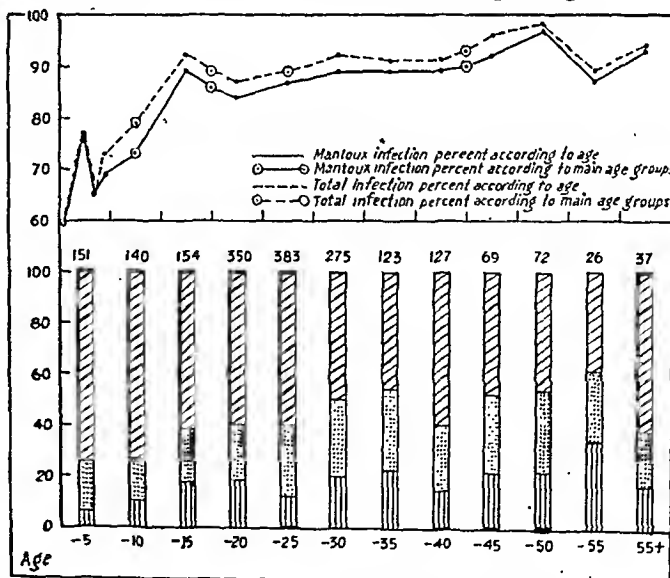
I. The urban survey at Serampore

Serampore with a population of about 50,000 is situated in the lower reaches of the

CHART I

Serampore town as a whole.

Distribution of 'Mantoux infection', intensities of reaction, and 'total infection' according to age.



Hooghly within the great industrial belt stretching along the river. It is richly supplied with communications by means of rail, road and river, and a big volume of suburban traffic passes through it. The tract of country in which the town is situated has an unenviable

record of morbidity and mortality from all causes, but, with its organized public services, the town itself enjoys better health conditions than the surrounding country. It has a mixed industrial and non-industrial population, and this was one of the main considerations which weighed in favour of its selection.

Since it was not possible to isolate the industrial from the non-industrial sections of the town, an arbitrary division into three categories of streets was made after a house to house survey, *viz*, 'civil', 'industrial' and 'mixed' according as there was a preponderance of one or the other type of resident (60 per cent or more). Actually there was 86 per cent non-industrial population in the 'civil' category and 85 per cent industrial population in the 'industrial' category. In the 'mixed' category there was a 37 per cent industrial population.

A sample of little over 5,000 persons was selected by Tippet's number technique for the purposes of the survey from streets of each category, but it was not found practicable to complete the work within the allotted period. Actually, only 2,552 individuals were included in the survey. Since, however, the proportions of families and of individuals in the final sample correspond with those found in the whole population as regards 'civil', 'industrial' and 'mixed' categories, reliance can be placed on the randomness and representative character of the population examined.

It may be mentioned in passing that our experience suggests that the staff recommended by the sub-committee for type I survey for 10,000 population is probably an underestimate. Under favourable circumstances, that staff will probably satisfactorily cope with only half the number.

Data were collected on the schedules given in the sub-committee's report. Two items in which modification is suggested by the present experience are (1) in classification of the 'occupation' and (2) in clinical classification of tuberculous persons.

The clinical classification according to stages, as suggested by the sub-committee for the classification of pulmonary tuberculosis, is perhaps too complicated for survey work, and it is suggested that Cummin's modification of Irvin's classification based on skiagraphic examination as given by Sen into 'nil', 'X', 'Y', and 'Z',^{*} with further subdivisions of active cases into 'open' and 'closed' will adequately serve the present purpose. This classification has been adopted in the present communication.

It may also be of interest to note that usual methods of propaganda through leaflets and magic lantern lectures did not prove successful.

Better results were obtained by enlisting the active co-operation of the medical practitioners, by establishing a branch of the Tuberculosis Association of Bengal, and by demonstrating the defects revealed in the course of clinical and radiological examinations to the relations of the patients.

Without prejudice to the significance of the response to the 'Mantoux' test, and of the 'X' and 'Y' cases as diagnosed by radiographical methods, it is convenient to use the term 'Mantoux infection rate' to denote response to the Mantoux test alone, and the term 'total infection rate' when the results of x-rays and of laboratory examinations have also been taken into consideration. The antigen used for the Mantoux test was O.T. 1 : 1,000 dilution in the first instance. In the case of non-reactors, a re-test was done with 1 : 100 dilution. We have also made use of the term 'tuberculous lesion' to include 'Y' and 'Z' types and also 'X' type, if in the latter case suspicious signs or symptoms were present, if there was history of contact, or if the subject reacted intensely to tuberculin. If only 'X' lesions are present the case is labelled as 'non-morbid tuberculous', but if there are active lesions (Y or Z) it is called 'morbid tuberculous'.

Incidence of infection

'Mantoux infection' was found in 85 per cent of the population and 'total infection' in 88 per cent. The lowest rates were found in the 'industrial category' but infection was not localized to any particular area, all parts of the town showing a high incidence (*vide* table I).

TABLE I
Distribution of infection in 42 out of 101 streets included in the survey, in which 20 or more persons were examined

Total infection rate	NUMBER OF STREETS	NUMBER OF STREETS IN DIFFERENT CATEGORIES		
	Total	Civil	Industrial	Mixed
70-	2	1	1	0
75-	6	4	1	1
80-	3	1	0	2
85-	8	4	2	2
90-	15	11	1	3
95-	8	3	1	4
	42	24	6	12

As is usual the 'Mantoux infection rate' increases with age (*see* table II) but a high incidence of infection at an early age is a significant feature of this community. Thus the infection rate for the 29 infants is 59 per cent, and it is as much as 68 per cent in children under 2 years. There is again a sudden rise in adolescence (11 to 15 years), the percentage being

* X, Y and Z = definite x-ray evidence of infection.
X = non-morbid, not active.
Y = morbid, probably active.
Z = certainly active.

as high as 89. The 'total infection' age curve follows closely the 'Mantoux infection' age curve. It would thus appear that even the 16 and 30 years of age, as against 41 per cent and 60 per cent in the 'civil' and 'mixed' categories respectively. On the other hand,

TABLE II

Distribution of 'Mantoux infection' intensities of reaction and 'total infection' in the town as a whole according to age groups

Age in years	Sample examined	Mantoux tested	MANTOUX INFECTION Per cent on sample tested	INTENSITIES OF REACTION				TOTAL INFECTION Per cent on sample examined
				1+	2+	3+	4+	
				Per cent	Per cent	Per cent	Per cent	
-1	29	29	59	82	18	nil	nil	59
-2	37	37	68	68	28	4	nil	68
-3	56	55	76	86	12	2	nil	77
-4	47	46	65	67	20	10	3.0	66
-5	55	54	69	70	19	11	nil	73
-10	202	193	73	73	16	11	nil	80
-15	194	174	89	62	21	18	nil	92
-20	478	415	84	60	22	18	nil	87
-25	510	443	87	60	28	12	0.3	89
-30	359	310	89	50	31	19	0.4	92
-35	170	139	89	45	33	23	nil	91
-40	161	143	89	60	25	14	0.8	91
-45	84	75	92	48	30	20	1.0	96
-50	86	74	97	46	32	21	1.0	98
-55	37	30	87	39	27	35	nil	89
55-	47	40	90	62	27	16	nil	94
	2,552	2,257	85	59	25	16	0.3	88

limited environment of the infant and young child is dangerously surcharged with infection.

The remark about infection amongst the infants is by no means limited to the industrial section, because a majority of the children belong to the 'civil' category of streets. The age constitution of the three categories of streets is, as may be expected, markedly at variance, 75 per cent of the population in the industrial category being young adults between

children below 7 years constitute only 7 per cent of the population in the 'industrial' category, as against 33 per cent of the 'civil'. Since it is a well-known epidemiological principle that all kinds of infection should be postponed, to a later period of life, if they cannot be avoided altogether, it is evident that measures required to prevent infants and children from getting infected are strongly indicated. In the earlier age periods, the proportion

TABLE III

Incidence of tuberculosis in the town as a whole and in different categories of streets

	Number in sample	TUBERCULOUS			
		Total (X, Y and Z) Per cent on sample	Non-morbid (X) Per cent on sample	Morbid (Y and Z)	
				All	Open only
				Per cent on sample	Per cent on sample
Civil ..	1,407	42	34	8	4
Industrial ..	536	17	14	4	1
Mixed ..	609	31	24	7	3
Town as a whole ..	2,552	34	27	7	3

TABLE VI

Incidence of tuberculosis (in the town as a whole and in the different categories of streets) classified according to sex and religious communities. (Percentages based on the number in the sample)

	TUBERCULOUS															
	Total (X, Y and Z)				Non-morbid (X)				Morbid (Y and Z)							
									All				Open only			
	Categories				Categories				Categories				Categories			
	Whole town	Civil	Ind.	Mixed	Whole town	Civil	Ind.	Mixed	Whole town	Civil	Ind.	Mixed	Whole town	Civil	Ind.	Mixed
	Per cent on sample				Per cent on sample				Per cent on sample				Per cent on sample			
Hindu male.	36	46	13	37	28	36	10	30	9	11	3	7	4	6	1	4
Hindu female.	41	45	23	32	35	39	18	21	7	6	5	11	3	3	3	4
Muslim male.	24	27	24	22	20	23	20	18	4	4	4	4	1	1	1	1
Muslim female.	21	18	15	44	15	14	10	25	6	4	5	19	5	4	5	6
Christian male.	47	56	nil	44	35	33	nil	36	12	22	nil	8	6	11	nil	4
Christian female.	33	45	nil	nil	27	36	nil	nil	7	9	nil	nil	7	9	nil	nil

TABLE VII

Distribution of 'total infection' in the two sexes amongst the three religious communities in the town and in different categories of streets. (Percentages based on the number in the sample)

	TOTAL INFECTION											
	WHOLE TOWN			CIVIL*			INDUSTRIAL			MIXED		
	Male	Female	Both sexes	Male	Female	Both sexes	Male	Female	Both sexes	Male	Female	Both sexes
Hindu ..	86	89	87	88	89	88	78	98	81	91	89	91
Muslim ..	89	85	89	88	85	87	93	85	92	97	88	87
Christian ..	97	81	92	89	82	85	nil	nil	nil	100	75	97
	87	89	88	88	88	88	84	93	85	90	88	90

regards the migratory population Ukil's* classification of habitat has been adopted. The 'Mantoux infection' rate in the four categories of population, viz, 'rural', 'semi-rural', 'urban changed' and 'urban unchanged', was found to be 76 per cent, 84 per cent, 85 per cent

and 85 per cent respectively.

The differences are brought out more clearly when similar age groups are considered (table VIII).

Thus taking the groups in the above order, the percentages of 'Mantoux infection' were

* Ukil's definition of habitat (personal communication).

Rural : domicile in a rural area, has not lived in a sparsely populated small town for more than one year or in a big and densely populated town for more than six months in the aggregate.

Semi-rural : domicile in a sparsely populated town or has not lived in a densely populated town for a period exceeding three years in the aggregate.

Urban : domicile in a densely populated city or has lived there for a period exceeding three years.

TABLE VIII

Town as a whole. Distribution of 'Mantoux infection' rate and intensities of reaction according to habitat and main age groups

Main age groups	NUMBER TESTED				MANTOUX INFECTION RATE			
	Rural	Semi-rural	Urban changed	Urban unchanged	Rural	Semi-rural	Urban changed	Urban unchanged
0-5	2	7	42	170	50	71	64	69
5-15	3	12	80	172	33	92	80	80
0-15	5	19	122	442	40	84	75	76
30	108	241	471	348	77	83	86	93
30-	10	18	213	260	80	100	91	90
	123	278	806	1,050	76	84	85	85

77, 83, 86 and 93 respectively, in the age groups 15 to 30 years. A similar grading was noted in 'tuberculous lesions' as seen in the skiagrams, the respective percentages being 20, 28, 30 and 40 (*vide* table IX).

lesions (whether active or not) in the various categories of the population for the 'urban unchanged' (9 per cent); on the other hand, in the 'rural' group as also in the 'urban changed' group there is a considerable varia-

TABLE IX

Incidence of tuberculosis (in the town as a whole and in different categories of streets), classified according to habitat. (Percentages based on the number in the sample)

	TUBERCULOUS															
	Total (X, Y and Z)								Morbid (Y and Z)							
					Non-morbid (X)				All				Open only			
	Categories				Categories				Categories				Categories			
	Town	Civil	Ind.	Mixed	Town	Civil	Ind.	Mixed	Town	Civil	Ind.	Mixed	Town	Civil	Ind.	Mixed
Rural	20	37	8	26	16	29	6	19	5	7	2	7	4	7	2	5
Semi-rural	28	46	10	32	26	45	8	30	2	1	2	2	nil	1	nil	nil
Urban changed.	30	36	22	31	25	30	19	23	6	6	3	8	3	3	1	4
Urban unchanged	40	45	20	32	31	35	11	24	9	9	9	9	4	5	2	3

Corresponding figures for active lesions are 5, 2, 6 and 9. The small figure of 2 in the semi-rural group is not readily understandable, for the size of the sample is fairly large, *viz*, 302. A point to note in this connection is that 4 per cent of the rural group—the same proportion as in the urban unchanged group—were open cases of tuberculosis. If, as one has reason to believe, they have acquired infection and disease in the town, and if they still retain connection with the village home, the evil effects of uncontrolled rural-urban contact can easily be imagined.

Another point of interest emerging out of these data is the constant rates of tuberculous

tion between the categories, the industrial categories showing the lowest rate. The most probable explanation of these findings is that the industrial workers return to their original homes when sick and thus disappear from the picture. If this surmise is correct, it will again point to the gravity of the situation arising out of uncontrolled industrialization.

Occupation

The expected findings regarding the influence of occupation as classified by the Tuberculosis Survey Sub-Committee, on the incidence of infection and disease, have not been made in the present investigation (*see* table X).

TABLE X

Distribution of 'Mantoux infection' rate and intensities of reaction and 'total infection' rate according to occupation in the town as a whole and in different categories of streets

Occupation	Sample examined	Sample tested	Percentages based on sample tested in each occupational group	1+	2+	3+	4+	Percentages based on sample tested in each occupational group
Outdoor ..	72	60	90	56	24	19	2	93
Indoor dusty ..	877	792	85	58	31	11	0.1	86
Indoor non-dusty ..	1,259	1,084	86	59	22	19	0.2	89
Contact ..	344	321	79	62	21	16	1	85

Thus with regard to 'Mantoux infection', the outdoor occupational groups show the highest rate, 90 per cent. Next in order are the indoor non-dusty occupations with a 'Mantoux infection' rate of 86 per cent; then comes the indoor dusty with a rate of 85 per cent, and finally the occupational contact group with 'Mantoux infection' rate of 79 per cent. That is to say, the order in regard to 'Mantoux infection' rate is almost reverse of what might have been expected. The same is true of the incidence of active lesions—the respective percentages being 14, 9, 5 and 3. Does this mean that (a) non-occupational environment is of greater significance than the occupational or (b) that the classification adopted by the sub-committee does not satisfactorily depict the risk? Reference has already been made to the suggested modification of the occupation classification. Moreover, it is possible that the factors of importance which have not or cannot be included in the 'principles of classification' are professional over-crowding and rapidity of change of contacts as, for instance, occurs in the case of a bus conductor under rather unfavourable conditions. Our expectation of incidences of infection and of disease in relation to occupation cannot, therefore, be inelastic. Familial contact with cases of tuberculosis, particularly if they are open cases, is generally believed to be the most fruitful source of infection and disease. This is in fact the reason why tracing contacts is an essential element in our anti-tuberculosis schemes. The present investigation fails to bring out in a conspicuous manner the importance of home contact in the dissemination of infection, as is evident from table XI.

TABLE XI

Infection rates amongst contacts and non-contacts

	Mantoux infection rate	Total infection rate
Contacts of active cases ..	85	90
Non-contacts ..	84	85

The difference in 'total infection rates', small as it is, may partly arise from the fact that in selecting subjects for radiographical examination, a history of contact has been taken as a criterion. No comparison in the morbidity rates can be made because the families included in the non-contact group are by definition free from active cases.

It may be argued that only the contacts of open cases are pertinent to this discussion. This may not be quite true, as the classification of active cases into open and closed on the basis of one or two sputum examinations is not very satisfactory. However, even such an analysis (see table XII) does not bring out as much difference as might be expected.

TABLE XII

Mantoux infection rate and total infection rate amongst contacts of open cases and non-contacts

	Mantoux infection rate	Total infection rate
Contacts of open cases ..	84	90
Non-contacts ..	84	85

However, a difference amongst the contacts and the non-contacts is seen in the intensity of reaction, a higher percentage of 3+ or more intense reactors is found in the contacts of active cases than in the non-contacts, the respective percentages being 20 and 13 (see table XIII).

This is probably an expression of higher doses and more frequent exposure to which the contacts are subjected. If so, it is reasonable to expect that morbidity rates amongst the two groups will also vary, but it cannot be demonstrated, as cases of tuberculosis amongst the latter group cannot exist by definition. The point to note, however, is that under conditions prevailing in the town, extra-familial sources are perhaps as important as the familial sources in spreading infection in the community.

TABLE XIII

Incidence of Mantoux infection and intensities of reaction amongst familial contacts of active cases and amongst non-contacts

	MANTOUX INFECTION		INTENSITIES OF REACTION (%)			
	Number tested	Per cent	1+	2+	3+	4+
Contacts of active cases ..	710	85	59	22	19	0.6
Non-contacts ..	1,380	84	59	28	13	0.2

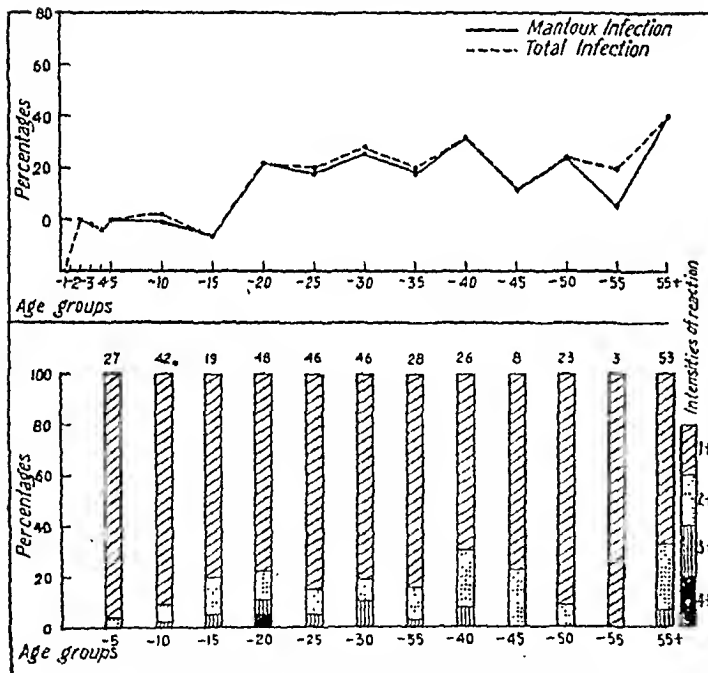
II. Barisal rural survey

The area investigated lies in the Gangetic delta within the bend of the Areal Khan River in the two-mile strip along the perimeter of Barisal town. Since the countryside is broken up by innumerable channels which are subject

CHART II

Barisal rural area.

Mantoux infection, total infection and intensities of reaction in the villages as a whole, and their distribution in different age groups (5 yearly age periods).



approximation between the actual and expected values on the basis of random distribution, in the different groups, irrespective of the nature of communications. The difference such as exists is mostly due to smaller number of women and children undertaking frequent journeys, especially with difficult transport facilities.

Originally it was proposed to include for purposes of the investigation the whole population of the four union boards comprising the strip of the country mentioned above. This was not found practicable. A sample had therefore to be taken. To begin with, the area included in the survey was limited to two union boards; the total population being 7,347. A sample was drawn by Tippet's number technique. It comprised of 1,121 individuals distributed in 250 families. Compared with the total population, the sample included a somewhat smaller number of persons from villages 'very easily approached' and comparatively more from the 'easily approached' group of villages. All the 1,121 persons of the sample were subjected to investigation, but 9 visitors have been excluded from the discussion.

Co-operation in the villages was of a passive nature, and for that reason few would consent to come over to the clinic in the town for purposes of radiological examination.

Incidence of infection

31 per cent of the 1,111 persons 'Mantoux tested' gave positive reactions. We are not in a position to calculate the total infection rate for this community in the absence of radiographical information, for a large number of persons due for x-ray examinations did not attend, but on the basis of information available the infection rate rises to at least 32 per cent. Compared with Serampore it is low, but even so it is high for a semi-isolated rural community.

It was seen in connection with the Serampore survey that the group of 'rural habitat' had a lower 'Mantoux infection rate' than the 'semi-rural', 'urban changed' and 'urban unchanged' groups. When compared with the Barisal rural group—which may be properly so called—the Serampore rural group exhibits almost double the infection rate. In fact it is about the same as in Barisal town (selected group) which is 76 per cent. Thus so far as

to tidal action, overland traffic is difficult, and communications with the town and surrounding country, such as there are, are mainly provided by the waterways. We are, therefore, dealing here with a semi-isolated community in marked contrast to Serampore. Moreover, the population being typically rural with practically no industries, there is little incentive to travel. That socio-economic or other human needs largely determine traffic are borne out by a perusal of table XIV.

It will be seen that while very difficult communication does to a certain extent discourage daily visits to the town, and relatively large number of persons so situated are found under group IV, there is in general a fairly close

TABLE XIV

Frequency of visits (in mutually exclusive groups) to Barisal town by the residents of the villages in different categories with regard to facilities of approach

Access	SAMPLE		GROUP I*		GROUP II		GROUP III		GROUP IV	
	Actual	Expected	Actual	Expected	Actual	Expected	Actual	Expected	Actual	Expected
Very easy ..	178	177	21	17	33	37	59	30	65	93
Easy ..	284	284	30	28	72	60	41	47	141	149
Difficult ..	323	317	38	32	53	67	56	55	176	170
Very difficult ..	327	337	20	32	74	68	31	55	202	172
	1,112	1,112	109	109	232	232	187	187	584	584

* Note.—Group I: Daily visits to Barisal town.

Group II: Visiting the town once a year or more frequently.

Group III: Visiting once or more frequently in two years.

Group IV: Less frequently than once in two years.

tubercularization of population is concerned, 'rural habitat' in the two instances has different meanings.

It would appear from table XV that the degree of tubercularization is directly related to the degree of contact with the town.

TABLE XV

Infection rates in groups mutually exclusive of Barisal rural population, classified according to the frequency of visits to the town

Groups	Number in sample	Percentage of Mantoux infection	Percentage of total infection
I. Daily visitors ..	109	48	50
II. Visiting more frequently than once a year ..	232	40	40
III. Visiting once or more often in two years ..	187	31	32
IV. Visiting less than once in two years ..	584	25	26
	1,112	31	32

What is surprising however is that even amongst very occasional visitors 26 per cent show evidence of infection. In most instances the visits to the town are not prolonged—rarely being more than 7 days in duration; usually they are only business-day visits, most of the time being spent in the open market place. Paisa (pie) hotels and cinema halls may provide greater exposure in some cases. If, as appears reasonable, it is permissible to assume from the morbidity rates in the villages (see below) that infection is mostly acquired in the town, the rapidity with which infection establishes itself amongst the rural population indicates widespread infection in the town, and a high degree of susceptibility of the village folk. Naturally, therefore, a relatively short sojourn in an urban area will suffice to change the rural community into an 'urban' one so far as incidence of infection is concerned. It must, however, be noted that the rapidity of change from the uninfected to the infected state suggested in the above discussion relates to contact with Barisal town and even more so to Serampore and presumably to other towns in Bengal similarly situated. It is not intended for general application. For instance, a comparison of 'Mantoux infection' rates as given in table XVI shows that school children in Sialkot

TABLE XVI

Distribution of 'Mantoux infection' rate and intensity of reaction amongst young persons at Barisal (rural), Sialkot (school) and Serampore

Places	Age groups	INTENSITY OF REACTION PERCENTAGES ON POSITIVES				Total tested	Mantoux infection rate
		1+	2+	3+	4+		
Barisal (rural) ..	5-20	82.56	11.00	4.58	1.83	454	24.00
Sialkot ..	5-18	76.95	16.99	5.12	0.92	6,436	33.63
Serampore ..	5-20	63.35	20.34	16.45	nil	782	82.35

(Punjab) exhibit a much lower 'Mantoux infection rate' than children of a more or less similar age in Barisal town and Serampore. The low rate in the Sialkot group may be partly due to a slightly lower range of age and partly to the fact that, being school children, they may represent perhaps a higher group in social status than the children drawn from the general population in Serampore, particularly the older children.

It may be of interest to note here the results of 'Mantoux tests' carried out in Barisal town in a girl and a boy school having 138 and 64 children respectively. The age group in both these cases was 5 to 20 years. The 'Mantoux infection rate' for girls was 54 per cent and for boys 48 per cent. Thus the children of Barisal town occupy a position intermediate between that of Sialkot and that of Serampore.

It is, however, conceivable that with varying incidence of infection in the town, and presumably differences in the distribution of infection, the rate of change with regard to infection in a rural community coming in contact with the town is likely to vary considerably. Thus the definition of rural habitat and the question of the influence of habitat on infection rates, especially if change of residence has been affected, are matters of some difficulty.

Morbid and non-morbid tuberculous rates in the Barisal rural population as a whole are subject to certain limitations. In the Serampore survey, a preliminary selection for radiographical examination was made through screening. For the Barisal group this method was not available for all people. As judged by the other three criteria mentioned in connection with the Serampore survey, 57 persons were selected; all the 11 with signs or symptoms agreed to x-ray examination, but only 10 out of 26 contacts and 12 out of 20 high reactors. It may be mentioned that 14 out of 16 contacts who could not be subjected to radiological examination were 'Mantoux negative'. Of the 33 actually examined, 27 showed non-morbid tuberculous lesions (X) and 4 exhibited active lesions. These latter were all with signs and symptoms. It is not possible to use these results for working rates, as 24 out of 54 eligible for examination were not skiagraphed. The only figures we have for comparison in the Serampore survey, therefore, are the numbers of X, Y and Z and nils amongst the 1,141 persons whose skiagraphs were taken. The data are set out in table XVII.

TABLE XVII

	Numbers skiagraphed	Non- TUBER- CULOUS	TUBERCULOUS	
		Nil	Non- morbid (X)	Morbid (Y and Z)
Serampore	1,141	285	699	157
Barisal	33	2	27	4

To the number of morbid tuberculous should be added 17 cases who being sputum-positive and clinically advanced cases of tuberculosis were not subjected to x-ray examination.

Unfortunately this comparison serves no useful purpose, but it is probable that no case of active tuberculosis was missed. On this reckoning it may be stated that morbidity in this group is low. It may therefore be concluded that, although certain contacts with the town provide for dissemination of infection amongst the rural population considered here in a surprisingly rapid manner, the resultant of the forces operating on them, whether related to dosage of infection or to environmental circumstances, is not favourable to the development of active lesions.

Perhaps a consideration of the distribution of intensities of 'Mantoux reaction' in the two surveys is relevant to the present discussion.

Table XVIII provides the necessary data for comparison.

TABLE XVIII

		INTENSITY OF REACTION			
		1+	2+	3+	4+
Serampore	..	59	25	16	0
Barisal (rural)	..	82	13	5	1

Note.—Actually the percentage of 4+ reactors for Serampore is 0.3 and for Barisal 0.6.

It would therefore appear that not only is the 'Mantoux infection rate' lower at Barisal than at Serampore, but the bulk of the positives in the rural area are mild reactors. If it is permissible to presume that these distributions, apart from other considerations, denote relative differences in the frequency and dosage of infection in the two areas, one reason for the higher morbidity rate at Serampore becomes evident. Another point of considerable interest brought out by a comparison of the data of the rural and the urban surveys is the difference in the 'Mantoux age curves' (see charts I and II).

Attention may be drawn to the two points in this connection: (1) the difference in the rates observed at -1 year and -2 years, and (2) the step-like manner in which the Barisal curve rises as compared to the more or less smooth curve at Serampore. These two peculiarities of the Barisal rural population are explicable on the ground that contact with the town is also correlated with age.

Thus the exposure of children in the rural area is much less than that of the adults.

Sex

Even though the females in the Barisal group are relatively younger in age and have much less contact with the town, the difference in the

incidence of 'Mantoux infection' in the two cases is not marked, the rate for the males being 33 as against 30 for the females. However, for some unknown reason, children under 15 years in group IV (that is, those visiting the town less frequently than once in two years) show a significant difference in the two sexes ($X^2 = 6.6$ $P = 0.0103$), the rate for the female being twice that of the male. Is it because the girls, once they have gone to the town, stay for many more days than the boys? We have no means of clearing up these points. The only point known in this connection is that a slightly larger number of girls than boys were in contact with active cases. This fact, however, could only partly explain the disparity observed here.

As at Serampore, so also in the Barisal rural area, the incidence of infection is somewhat lower amongst the Hindus than amongst the Muslims. This disparity cannot arise from such differences as exist between the two communities in contact with the town; these factors, if anything, weighed against the Hindus. Are differences due to social status?

The outdoor occupations exhibit a higher rate of infection than the indoor occupations, but the explanation is provided by the fact that the former group is more in contact with the town and includes a proportionately larger number of older people.

tuberculous rate works out to be 76 per cent. This figure closely approximates to that of Serampore (75.5 per cent). These findings, curious though they appear, signify a wide prevalence of unknown sources of infection diffused in the community.

Summary and conclusions

Type I and type II surveys have been carried out in an industrialized urban area near Calcutta (Serampore) and in a rural area (on the outskirts of Barisal town) on the lines suggested by the Tuberculosis Survey Subcommittee of the Indian Research Fund Association.

Infection rates as judged by 'Mantoux test' and by radiographical examination were as high as 88 per cent in the urban area and 32 per cent in the rural area. Tuberculous lesions (X, Y or Z) were found in over one-third of the population (34 per cent) and active lesions (Y or Z) were observed in 7 per cent of the population in Serampore. What is however more serious is that 3 per cent of the population definitely constitute sources of infection. These figures, though not strictly comparable with those found by Dr. Ukil as a result of his post-mortem studies on subjects of accidental deaths in Calcutta, are closely similar to them, and these facts portray a serious situation as regards tuberculosis

TABLE XIX
The results of radiographical examinations

Reason for examination	Total number	Number examined	Nil	Tuberculous lesions	
				X	Y and Z
Suspicious signs and symptoms	11	11	0	7	4
Contact history ..	26	10	2	8	0
High Mantoux reaction ..	20	12	0	12	0
Other Mantoux positives ..	313	76	5	71	0
	370	109	7	98	4

A general discussion of tuberculous lesions has already been given. Actually many more than the 57 individuals mentioned before were radiographically examined (see table XIX).

In Barisal town the results of a rough survey throw some light on the position of tuberculosis infection and morbidity. Two hundred and ninety-six contacts of 43 diagnosed tuberculosis cases attending the clinic were investigated under the x-rays, and 75 per cent of them were found 'tuberculous' but only four of them showed active lesions. There was no open case. In a group of 78 persons belonging to 17 non-contact families selected at random and similarly investigated, the 'tuberculous' rate was 82 per cent. Taking both groups together, the

in and around Calcutta. A point of particular significance in this connection is the early age at which infection occurs, as seen from the infection rate amongst infants under one year of age which was 59 per cent, and it rapidly rose to 68 per cent in the second year of life. These findings call for strenuous measures designed to lower the rates of infection particularly in tender years.

It is also evident that the risk of infection apart from professional or domestic contact with tuberculous patients is not inconsiderable. There is in fact evidence to suggest that this susceptible rural population may pick up infection during casual visits to the town.

(Concluded on next page)

GENERAL HOSPITALS AND PULMONARY TUBERCULOSIS

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SHOULD a general hospital have a tuberculosis ward with adequate facilities for diagnosis and treatment, or should all tuberculosis patients be necessarily looked after only in separate tuberculosis institutions?

As one with ten years' experience in tuberculosis work, half of which has been gained in separate institutions for the tuberculous and the other half in general hospitals with tuberculosis departments within their precincts, I feel justified in attempting to answer the above question.

To start with, let me take the objections that may be raised against having a tuberculosis department inside a general hospital.

(1) The fear that the public and other patients in the hospital would object to the presence of tuberculosis patients in the same premises.

(2) The danger of exposure of the hospital personnel to infection.

(Continued from previous page)

The intensity of the Mantoux reaction and the morbidity on the other hand appear to be related to frequency and dosage of infection. More detailed surveys (type III) designed to demonstrate sources and circumstances responsible for a high degree of diffusibility of infections in the towns are indicated. Tuberculosis would appear to be essentially a problem of urban communities in Bengal, and such extension as takes place in the rural areas is due to contact with the towns. Hence uncontrolled urbanization and industrialization are fraught with danger. This could be largely met by concentrated attention on urban tuberculosis, but it appears doubtful whether measures designed solely to trace and manage familial contacts will materially control infection.

Acknowledgments

To Lieut.-Col. A. C. Chatterjee, I.M.S., the then Director of Public Health, Bengal, is due the credit of inaugurating the surveys and finding the means to carry them out. We are indebted to Dr. B. Mukherjee, Officiating Director of Public Health, Bengal, for giving all the facilities for completion of the paper. For technical assistance, we are grateful to Drs. A. C. Ukil and P. K. Sen, who read through the manuscript and made many useful suggestions. Dr. P. K. Sen kindly collaborated by reading the skiagrams and giving us the benefit of his interpretations and classifications of cases. To many leaders of the public, both official and non-official, we express our grateful thanks for helping in organization, for enlisting co-operation, and for raising funds for x-ray apparatus at Serampore.

The answer to both the above objections is the indisputable fact that quite a number of unrecognized tuberculosis patients are unwittingly admitted into the general wards, and it is obviously an advantage to have a portion of the hospital kept ready immediately to segregate such cases as soon as they are discovered to be tuberculous. And once in the tuberculosis wards, adequate care will be taken for the proper collection and disposal of the sputum. Thus a tuberculosis ward is more likely to provide increased protection to the patients and the staff of a general hospital.

(3) A third reason that may be advanced against treating tuberculosis patients in general hospitals is that a sanatorium climate and regimen cannot be supplied in a city hospital. This question I have discussed in detail elsewhere (Sanjivi, 1937) and it does not require much effort to prove that, given facilities for collapse therapy, the luxury of a special climate is not essential for recovery from tuberculosis.

As against the above possible objections, let me state the advantages of combining tuberculosis work with the other departments of a general hospital.

(1) The immense saving of money that is effected by providing facilities for the modern treatment of tuberculosis near the patient's house so that poor patients can be admitted at short notice, kept a few weeks and allowed to return to their work while attending for artificial pneumothorax refills for the optimum period of three years.

(2) The greater opportunities that will thus be provided for the immediate segregation of the open case from his usually unhealthy and overcrowded house.

(3) The possibility of combining field work such as examination of contacts and organized home treatment with institutional care, which will be rendered impossible by locating tuberculosis institutions far away from the patients' homes. It is time that the health departments of city municipalities came forward to do their share of work in the control of tuberculosis (Rajagopalan and Sanjivi, 1941).

(4) I have noticed that patients with really early lesions come more frequently to a general hospital for diagnosis, while it is only the patient with established disease, which unfortunately in this country means so often advanced disease, that seeks admission into a separate institution for the tuberculous.

The following notes are of three patients seen in a general hospital:—

Case 1.—Ramalingam, Hindu male, 27 years, had been admitted and investigated for abdominal symptoms suggestive of peptic ulcer with negative results. There were none of the usual symptoms associated with respiratory disease, such as cough, expectoration, fever, etc. Physical examination showed diminished air entry below the right clavicle and no other evidence of disease such as impaired resonance or crepitations. An x-ray of the chest (figure 1, plate XXIII) showed a typical Asman's focus.

Case 2.—Kelappan, Hindu male, 30 years, was admitted into the Evacuee Ward as a case of (?) malaria. As there was no evidence of malaria and he had a persistent cough with few physical signs, an x-ray of the chest was taken and it showed the typical Assman's focus (figure 2, plate XXIII). The sedimentation rate was 35 mm. in 1 hour and, although the sputum and gastric juice were repeatedly negative for tubercle bacilli, he was treated as a case of tuberculosis with improvement.

Case 3.—Mani, Hindu male, 16 years, was first admitted in June 1942 for pain in the right chest. X-ray (figure 3, plate XXIII) taken then showed, besides the pleurisy at the right base, diffuse peribronchial striations in the right subclavicular zone. The sputum was negative and he was discharged. He was readmitted in August 1942 with more definite exudative foci (figure 4, plate XXIII) in the right subclavicular zone and a positive sputum.

Such cases as shown in case-histories 1 and 2 seldom reach a tuberculosis hospital in that stage. Case-history 3 is an example of 'early spreading peri-bronchial granuloma' for the recognition of which I have pleaded in a previous paper (Sanjivi, 1939).

The above three cases are given as typical of a large number of similar early cases I have had while working in general hospitals. The number of these early cases will show a remarkable increase as soon as a physician specially interested in chest diseases begins to attend the out-patient department and help in the quiet and careful examination of both the new cases that appear suspicious and the old cases of 'cough' and 'bronchitis' which fail to respond to ordinary treatment carried out for over two weeks.

If there is no provision whatever for treating these early cases in general hospitals, they would have to be directed to go to a tuberculosis hospital or sanatorium, and quite often our poor, illiterate patients do not take the trouble to knock at another door (particularly when they do not have many obtrusive symptoms and do not understand the gravity of the disease) but put off all treatment to a stage when their condition becomes unbearable and untreatable. It may be argued that once we have advised them correctly it is not our fault if they do not follow the advice; but is a layman to be given capital punishment for not understanding the seriousness of neglected tuberculosis?

(5) Many non-tuberculous respiratory diseases are met with in the general wards and quite often their proper labelling gives rise to difficulties. In this connection case-history 4 is given as an example of a large abscess of the lung which has healed completely with x-ray therapy.

Case 4.—Narayanaswami, Hindu male, 32 years, was admitted for cough and spitting of blood of a month's duration. Physical examination revealed clubbing of the fingers and signs of a cavity in the right upper zone. Figure 5, plate XXIII, shows the x-ray appearances on admission. Sputum was repeatedly negative and a diagnosis of non-tuberculous lung abscess was made on the clinical features. Figure 6, plate XXIII, taken after a course of deep x-ray therapy shows the marked regression of the lesion.

This example has been cited here merely to prove the great importance of diagnosing a non-

tuberculous abscess as such, especially as we seem to have in x-ray therapy a good weapon for dealing with them.

It is essential that the diagnosis of pulmonary tuberculosis should be made after a careful consideration of (a) patient's symptoms, (b) physical signs, (c) the radiograph and (d) the examination of the sputum; whenever these cannot be properly correlated, the diagnosis must be questioned. For example, when the x-ray suggests caseo-pneumonic tuberculosis and the sputum is repeatedly negative, it is worth while remembering that the only types of tuberculosis in which the demonstration of the tubercle bacillus may be difficult are fibroid phthisis and miliary tuberculosis, and to carry out further investigations to see if an actinomycosis or a bronchial carcinoma may be responsible for the lesions in the lung. Case-histories 5 and 6 are instances where the sputum was repeatedly positive, and the x-rays showed no gross lesion, and we, therefore, made further 'sample' radiographic studies and established that a single picture may not always be infallible.

Case 5.—Subbanna Gounder, Hindu male, 23 years, was admitted into the surgical ward for discharging sinuses in the scrotum. As he had a cough, and physical signs were few (slight impairment of resonance and weak breath sounds at the left apex), an x-ray of the chest was taken (figure 7, plate XXIV). While the picture showed only increased density over the inner end of the left clavicle, the sputum showed tubercle bacilli. A sample skiagram of the left upper zone with displacement of the clavicle showed a definite cavity (figure 8, plate XXIV). Artificial pneumothorax failed in three spots indicating that it is impossible to be sure from a skiagram whether AP induction will be possible or not.

Case 6.—Pattu, Hindu female, 29 years, was admitted with a history of fever and pain in right side of the chest of less than a week's duration. Examination showed impaired resonance over the right base with weak breath sounds and a pleural friction sound. After a few days, the friction sound gave place to rather coarse râles but no alteration in the character of the breath sounds was noticeable. On x-ray (figure 9, plate XXIV) a slight haziness of the right base and a few soft patches at the right cardiophrenic angle were seen. The sputum contained many tubercle bacilli on successive days. As the x-ray appearance was not considered adequate to explain the sputum findings, another picture was taken displacing the right breast and using the Potter-Bucky diaphragm, with the result that a cavity at the extreme base was demonstrated (figure 10, plate XXIV).

Perhaps a realization of the need for weighing all the four data stated above and a refusal to rest satisfied until every case is properly labelled, will result in a more frequent diagnosis of non-tuberculous conditions such as bronchial carcinoma, actinomycosis and sarcoidosis as well as of occult tuberculosis.

Case-history 7 illustrates the difficulty of physical diagnosis in miliary tuberculosis.

Case 7.—Sabjan, Mohammedan male, 12 years, was sent from the Leper Settlement, Tirumani, for investigation of his continuous fever, with enlargement of the liver, and spleen just palpable. He had practically no cough and very little expectoration. Apart from the evidence of general toxæmia, the physical signs were few. In the respiratory system, percussion revealed a diffuse hyper-resonance and auscultation

revealed scattered crepitations. X-ray (figure 11, plate XXIV) showed a typical miliary involvement.

Where normal lung resonance gives place to a diffuse hyper-resonance in a person in the toxic typhoid state of miliary tuberculosis, it is invariably necessary to take an x-ray of the chest.

Case-report 8 shows how difficult it is to distinguish an 'eosinophilic lung' from miliary tuberculosis by the radiograph alone, and how necessary it is that no single factor should decide the diagnosis of tuberculosis.

Case 8.—Sivasami, Hindu male, 28 years, was admitted for cough and slight rise of temperature towards the evenings for one month. Figure 12, plate XXIV, shows the x-ray of the chest, the report of the radiologist on which was 'scattered soft patches both sides'. The sputum was repeatedly negative; the general health good; and the differential count showed 41 per cent eosinophiles. He responded well to anti-asthmatic measures.

Again, in cases 9 and 10, in which the patients ran an unexplained fever with basal signs immediately after laparotomy, the sputum examination was the first to establish the proper diagnosis of tuberculosis.

Case 9.—Govindasami, Hindu male, 31 years, was operated on for duodenal ulcer on 4th March, 1942. From the 22nd day after operation he was running an unexplained temperature. The signs of consolidation over the right base were put down to post-operative pneumonia. Widal and blood culture proved negative. An x-ray was taken of the chest (figure 13, plate XXV). The appearance was characteristic of caseo-pneumonic tuberculosis, and tubercle bacilli were discovered in the sputum. The patient was immediately transferred to the tuberculosis ward and artificial pneumothorax was started with good results.

Case 10.—Negappan, Hindu male, 30 years, was operated on for duodenal ulcer on 24th August, 1942. Developed cough with copious expectoration about the end of the first week after operation. Denied any previous history suggestive of pulmonary tuberculosis. X-ray taken on 11th September, 1942 (figure 14, plate XXV), showed consolidation of left base. The bacteriological origin of the consolidation was established by finding tubercle bacilli in the sputum. Artificial pneumothorax was started immediately, with much benefit.

(6) If we consider the large number of non-pulmonary tuberculous affections that are treated in a general hospital and the probability of some of them having co-existent pulmonary lesions which require simultaneous treatment, the inadvisability of rigidly excluding pulmonary tuberculosis from general hospitals will become obvious.

(7) A few specialists in large sanatoria may be able to do their own major surgical work such as thoracoplasty. But the clinic medical officer engaged mostly in spotting cases of tuberculosis and having but a few beds for their immediate treatment, will find the equipment and the experienced surgeons of a general hospital of valuable help in dealing with cases requiring major surgery.

(8) The final advantage in having a tuberculosis department in general hospitals attached to medical colleges is to teach the senior students at least two important facts about tuberculosis,

which cannot be so effectively taught in separate institutions, facts which it is so essential for the future general practitioner to learn. These are:—

(1) the principles of diagnosing tuberculosis in its truly early stages, and

(2) the confidence that pneumothorax refills are quite easy to give.

The failure to instil this confidence is blocking the progress of the treatment of tuberculosis to an extent not realized by most people. Outside Madras there are hardly a dozen centres in the Presidency where pneumothorax treatment is given, and patients have often to travel more than a hundred miles to get a refill. A well-established pneumothorax continued for three years is our surest weapon for treating tuberculosis. While the decision to induce pneumothorax and its initial induction must be left to these centres with specially trained men and radiographic facilities, its continuance by general practitioners in even remote villages is not impossible; in such cases it will suffice if the patient goes to the tuberculosis centre once in about six months, unless some complication supervenes.

My thanks are due to Lieut.-Colonel G. R. McRobert, M.D., F.R.C.P., I.M.S., Superintendent, General Hospital, for facilities in preparing and permission to publish this paper.

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DESCRIPTIONS OF ILLUSTRATIONS (PLATES XXIII–XXV).

- Fig. 1.—Case 1. Showing a typical Assman's focus in the chest.
Fig. 2.—Case 2. Showing a typical Assman's focus.
Fig. 3.—Case 3. Showing pleurisy at the right base together with diffuse peribronchial striations in the right subclavian zone.
Fig. 4.—Case 3. Showing more definite exudative foci in the right subclavian zone.
Fig. 5.—Case 4. Showing x-ray appearances on admission. Signs of cavity in the right upper zone.
Fig. 6.—Case 4. Showing marked regression of the lesion.
Fig. 7.—Case 5. Showing increased density over the inner end of the left cavicle.
Fig. 8.—Case 5. Showing definite cavity.
Fig. 9.—Case 6. Showing slight haziness of the right base and soft patches at the right cardio-phrenic angle.
Fig. 10.—Case 6. Showing a cavity at the extreme base.
Fig. 11.—Case 7. Showing a typical miliary involvement.
Fig. 12.—Case 8. Showing scattered soft patches—both sides.
Fig. 13.—Case 9. Showing characteristic appearance of caseo-pneumonic tuberculosis.
Fig. 14.—Case 10. Showing consolidation of the left base.

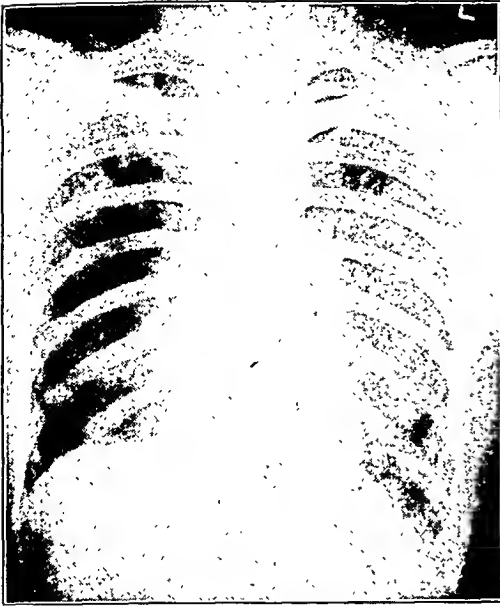


Fig. 1. Case 1.

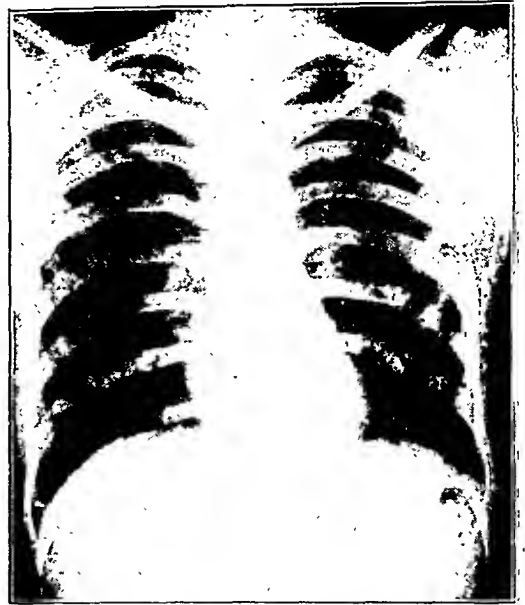


Fig. 2. Case 2.



Fig. 3. Case 3.



Fig. 4. Case 3.



Fig. 5. Case 4.

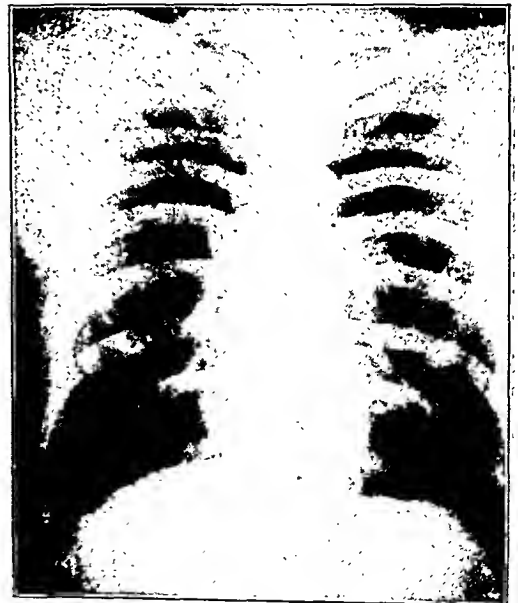


Fig. 6. Case 4.

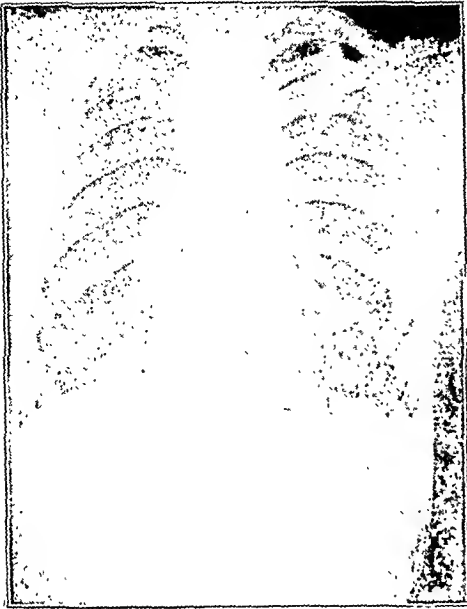


Fig. 7. Case 5.



Fig. 8. Case 5.



Fig. 9. Case 6.



Fig. 10. Case 6.

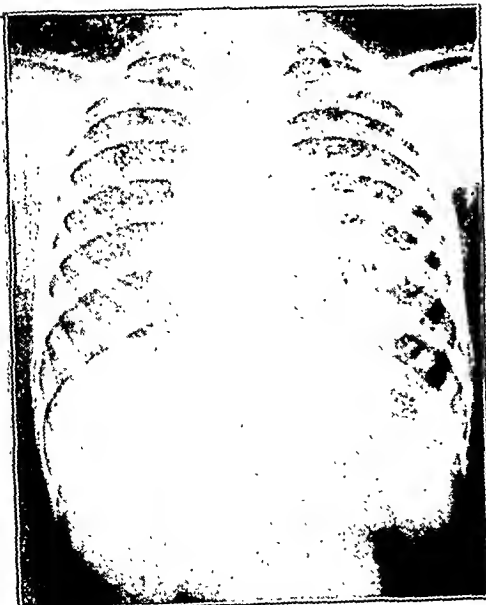


Fig. 11. Case 7.



Fig. 12. Case 8.

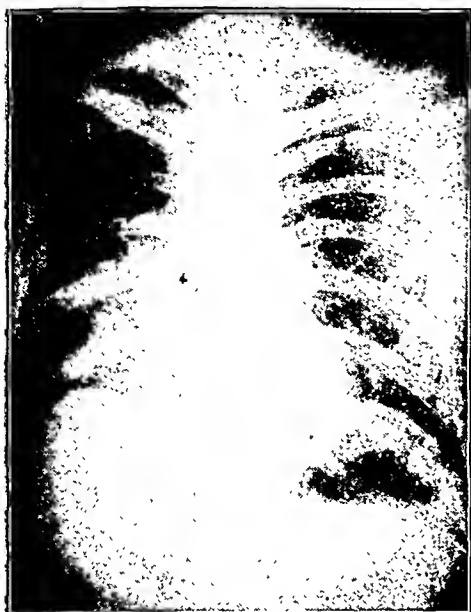


Fig. 13. Case 9.



Fig. 14. Case 10.

INTESTINAL TUBERCULOSIS : J. FRIMODT-MÖLLER



Fig. 2. Case 1.



Fig. 3. Case 1.



Fig. 4. Case 1.



Fig. 5. Case 2.



Fig. 6. Case 3.

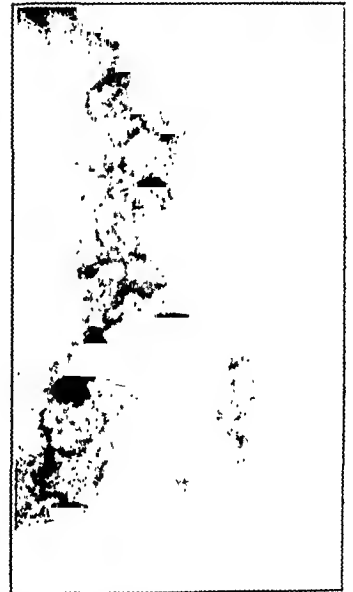


Fig. 7. Case 4.



Fig. 8. Normal case.

STOMACH-WASH EXAMINATIONS FOR TUBERCLE BACILLI

A REPORT OF 500 EXAMINATIONS

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IN 1898, Meunier demonstrated tubercle bacilli in the stomach-wash water of tuberculous children, but for about 30 years afterwards no use was made of this discovery. In recent years, however, its value has been increasingly recognized.

At first, gastric lavage was used for children in whom it is often difficult to get satisfactory specimens of sputum. Collis and Brockington (1933) give a brief summary of some of the early work, quoting examples from France, Denmark and the U.S.A. Among the workers quoted may be mentioned Armand-Delille and Vibert (1927) who found 34 positive stomach washes in 110 children suspected of having tuberculosis, and Armand-Delille (1930) who, in 500 children, found 100 per cent positive of those with physical and x-ray signs of caseous broncho-pneumonia and 60 per cent positive of those showing an x-ray picture suggestive of pulmonary tuberculosis. Levin (1934), dealing with a series of 457 children, found tubercle bacilli in the stomach wash in 70 per cent of those with active pulmonary tuberculosis or with pulmonary glandular lesions, in 76 per cent of those with radiological parenchymatous lesions in the primary and disseminative stages, in 97 per cent of those with the tertiary or adult type of disease, in 55 per cent when x-ray showed only tracheo-bronchial enlargement with perihilar shadows, and in 25 per cent without perihilar shadows.

From children the method was applied to adults. Gullbring and Levin (1937), reporting on a series of 461 adults, of whom 348 were tuberculous patients classed as sputum negative by direct and antiformin methods or having no sputum, and using both guinea-pig and culture methods, found that 192 of the 348 or 55 per cent had tubercle bacilli in the stomach wash made on three successive mornings. Stadnichenko and Cohen (1937) dealing with a series of 600 patients in their sanatorium, found 46 per cent positive by guinea-pig inoculation of untreated stomach-wash water of those with clinical tuberculosis but who had never had a positive sputum. Stadnichenko, Cohen and Sweany (1940) report on a series of 1,000 consecutive stomach-wash examinations with a technique similar to that of 1937 series. In this study, 213 patients who had never had a positive sputum were positive by stomach wash; 36 who later had a positive sputum were all positive by stomach wash; 94 who had had a positive sputum not less than 9 months earlier were positive; 159, of whom 139 had been sputum positive and 20 stomach wash positive, were negative; and 262 diagnosed as

tuberculous by clinical or x-ray examination or both, were negative by stomach wash; the remainder were positive and negative controls.

Many other smaller series of both children and adults have been reported on from Europe and America, proving the value of the method.

The source of the bacilli

The tubercle bacilli in the stomach may come from coughed up and swallowed sputum, or as has been suggested by Ulmar and Ornstein (1933) after demonstration by lipiodol and x-ray, from secretion swallowed as a result of bronchial peristaltic movement. Other sources have been suggested such as foci in the tonsils or nasopharynx, but bacilli from such lesions cannot form a large number of the positives. Bacilli secreted with bile and regurgitated into the stomach have been suggested as a source, but elimination of bacilli *via* the bile duct is not proven, at least in human beings, although Calmette (1923) reports that it occurs in cattle.

Series under review

The present series of examinations reviewed is a series of 500 consecutive stomach-wash examinations made in the Union Mission Tuberculosis Sanatorium, Arogyavaram, between September 1939 and June 1943, except for two isolated examinations made in 1938. The 500 examinations were made in 448 patients, 39 patients having 2, 5 having 3 and one having 4 gastric lavages at intervals during treatment. Of the whole series of patients, 4 only were children; 33 were Europeans, 18 Anglo-Indians, 449 Indians.

All the patients were admitted to the Sanatorium either after a diagnosis of tuberculosis had been established, or for consultation and observation when the diagnosis was in doubt. If, after the examination of direct smears of sputum on four consecutive days after admission, no tubercle bacilli were found, a sputum culture for tubercle bacilli was carried out and in many a stomach-wash culture also. Later, during treatment, generally after a minimum of three months of negative sputum examinations by direct smears four times a month, stomach-wash cultures were done in a number of patients, and on discharge after a similar period of negative direct smears.

Technique

The technique employed in this series was as follows: In the early morning before any food or drink was taken, the contents of the stomach were aspirated through a Ryle's stomach-tube and a large syringe. Sterile water was run in through the tube, the water was aspirated and reinjected a few times by means of the syringe, and was finally withdrawn, the total quantity of aspirated stomach contents and water being about 120 to 150 c.c. The stomach-wash water was then allowed to settle for several hours; the lower part only was taken and mixed with an

equal quantity of 6 per cent sulphuric acid (by volume), left for 20 minutes and then centrifuged at high speed for 20 minutes. The sediment was then washed with sterile water, recentrifuged, and was sown on six tubes of Jensen-Lowenstein medium* for each specimen: a little of the sediment was examined microscopically. The culture tubes were examined weekly for six weeks, and, if no microscopic growth was observed in that time, were reported negative, although the tubes were usually kept two weeks longer. Tubes showing typical colonies, with the bacilli showing typical staining and appearance microscopically, were reported positive. All glassware used in the tests were sterilized before use, and the Ryle's tube was boiled. Only one stomach-wash specimen was taken from each patient, i.e. specimens on three consecutive days were not pooled as is done in some institutions in the West. Centrifuge tubes holding 25 c.c. were used, one for each patient.

The group of non-pulmonary tuberculosis included 9 cases of tuberculous adenitis, 8 of intestinal and abdominal tuberculosis, 1 with tuberculous spine and 1 with tuberculous iritis.

The non-tuberculous group included the following patients:—

No active tuberculosis	79	Malaria ..	4
No tuberculosis	19	Syphilis ..	3
Non-tuberculous lung disease associated with eosinophilia	21	Gastritis ..	2
Bronchiectasis	7	V.D.H. ..	1
Lung abscess	5	Typhoid ..	1
Bronchitis	1	Diabetes ..	1
Asthma	1	Avitaminosis	1
Actinomycosis of lung	2		
Non-tuberculous lobar pneumonia	2		
Non-tuberculous broncho-pneumonia	1		
Non-tuberculous pleurisy	2		

As it is of some interest to know at what stage of the disease and at what stage of the treatment

TABLE I
Results of stomach-wash examinations according to diagnosis

	Culture positive	Smear only positive	Culture negative	Smear negative, culture contaminated	Total
Pulmonary tuberculosis ..	49	4	260	15	328
Non-pulmonary tuberculosis ..	0	(1)*	17	2	19
No active tuberculosis ..	0	(1)†	148	5	153
No disease ..					
No tuberculous disease ..					
TOTAL ..	49	4 (2)	425	22	500

* In one specimen 2 acid-fast bacilli were found after a long search, and culture showed no growth.

† In one case diagnosed as 'no active tuberculosis' a few acid-fast bacilli were found in the smear; culture showed no growth.

Results

In the whole series of 500 examinations, tubercle bacilli were found in 53, in 8 by smear examination, in 49 by culture, 4 being found only by smear examination. Of these 4, 1 was in a patient having a gastric analysis just before leaving the sanatorium; he had had a positive sputum earlier in his stay, and acid-fast bacilli assumed to be tubercle bacilli were fairly numerous in the smear of the fasting stomach-contents; in 2 patients who had some difficulty in swallowing the tube, a small pellet of sputum was coughed or vomited up, and on examination contained tubercle bacilli on smear, while the rest of the contents showed no bacilli on smear or culture; in 1 patient the smear showed acid-fast bacilli, but no growth was obtained although a sputum culture at the same time was positive.

The findings for the whole series are given in Table I, arranged according to the diagnosis.

* Asparagine had to be omitted from the medium in a fairly large proportion of examinations owing to the difficulty of getting it during the war.

the stomach wash was done, this question is examined in table II where the results are analysed according to the stage of the disease (the stages being those accepted by the Tuberculosis Association of India in its Report on Classification) and according to whether the stomach wash was done on admission, during treatment or on discharge.

It is also of interest to compare the results of stomach-wash examination with sputum examination in the patients suffering from pulmonary tuberculosis; table III gives the figures for the whole series of 328 patients, and table IV for patients on admission only. The sputum cultures are considered as having been made at the same time if done within a month of the stomach wash; most of them were done within a few days and a number on the same day. Sputum cultures were done if the patient on admission showed no tubercle bacilli in a series of four direct smears, and during treatment and on discharge usually after the patient had had four negative direct smears in each of three

TABLE II

Results of stomach-wash examinations in tuberculous patients according to stage of disease and stage of treatment

Stage of disease	Stage of treatment	Culture positive	Smear only positive	Culture negative	Smear negative, culture contaminated	Total
I	Admission	6	0	80	8	94
	During treatment	1	0	4	0	5
	Discharge	0	0	9	0	9
	Total	7	0	93	8	108
II	Admission	16	2	43	0	61
	During treatment	1	0	12	0	13
	Discharge	0	0	10	1	11
	Total	17	2	65	1	85
III	Admission	18	1	47	4	70
	During treatment	3	0	27	1	31
	Discharge	4	1	28	1	34
	Total	25	2	102	6	135
All stages	GRAND TOTAL	49	4	260	15	328

TABLE III

Stomach-wash examinations in relation to sputum examinations in tuberculous patients

Stomach wash	SPUTUM					Total
	Culture +ve	Culture -ve	Direct smears -ve	No sputum	Direct smear +ve	
Culture positive	12	21	15	0	1	49
Smear only positive	1	2	1	0	0	4
Culture negative	20	172	67	1	0	260
Smear negative	3	8	4	0	0	15
Culture contaminated	3	8	4	0	0	15
TOTAL	36	203	87	1	1	328

TABLE IV

Stomach-wash examinations as compared with sputum immediate and later examinations according to stage of disease in tuberculous patients

Stomach wash on admission	Immediate sputum culture	Later sputum culture	STAGE OF DISEASE			Total
			I	II	III	
+	+	..	2	1	8	11
+	+	..	2	14	10	26
+	+	+	2	3	1	6
-	+	..	3	4	8	15
-	-	+	2	4	15	21
-	-	-	75	35	24	134
			86	61	66	213

Twelve contaminated stomach-wash cultures were omitted.

consecutive months. A smear was made of the sputum sediment cultured, but very few of these were positive.

Discussion

In the whole series of 500 patients, 53 or 10.6 per cent were positive by stomach wash, 9.8 per cent by culture and 0.8 per cent by direct smear only; in addition, 4 or 0.8 per cent of the specimens cultured were positive also on direct smear; 1 specimen in the non-pulmonary group and 1 in the 'no active tuberculosis' group showed a few acid-fast bacilli in smears. It is known that acid-fast bacilli other than tubercle may occasionally be found in the stomach and a number of such have been found in this series of stomach-wash and sputum cultures; 1 specimen showed an equal number of colonies of tubercle bacilli and of an acid-fast saprophyte.

In the group of 143 patients classified as having no active tuberculosis, no tuberculosis at all, or having other diseases, the negative stomach-wash examination was only one of the factors in the diagnosis. The history, clinical symptoms, physical and x-ray examinations and the Mantoux test were other factors, together with any positive laboratory findings indicating other diseases. A negative stomach wash by itself would not rule out a diagnosis of active tuberculosis as can be seen from the number of patients diagnosed as having pulmonary tuberculosis and yet having both negative stomach-wash and sputum examinations.

Turning to table III and omitting those with contaminated stomach-wash cultures, we find 53 or 16.9 per cent positive stomach washes in patients whose sputum was negative by a series of direct smear examinations; in all of these the concentration material used for culture was negative on smear also. In stage I, 6 or 7.0 per cent of 86 patients with negative sputum examination on admission were positive by stomach-wash culture; in stage II, 18 or 29.5 per cent of 61 patients 'sputum negative' by culture and smear, and in stage III, 19 or 28.8 per cent of 66 patients sputum negative by culture and smear; stage II and stage III patients were about equal. On discharge the stage I and stage II patients examined were all negative, but stage III patients still showed 5 of 34 positive on stomach wash.

A question arises as to how it is that so many stage III patients did not show tubercle bacilli in the stomach wash on admission. An examination of the 47 negative stomach-wash stage III patients shows the following:—

Arrived with artificial pneumothorax ..	9
Arrived with unilateral or bilateral pleurisy ..	10
Patients with old fibrotic lesions ..	3
Patients whose staging was affected by complications, pregnancy, glandular and intestinal tuberculosis, i.e. lung condition not very advanced ..	3
Patient with small scattered foci ..	1
Patient provisionally placed in stage III with history of +ve sputum and artificial pneumothorax but Mantoux negative (1 in 10) ..	1

Of the above patients, 7 of the 9 arriving with artificial pneumothorax had a previous history of a positive sputum; 2 later became positive in the sanatorium. Of the pleurisy cases, 4 had tubercle bacilli in the pleural fluid and 2 were negative; 4 were not examined; 1 of these cases became sputum positive later. The case with intestinal complications also became sputum-positive later. In addition to these 4 who became positive later, 8 other patients were sputum culture positive on admission and 12 became sputum positive later. Stadnichenko *et al.* (1940) also comment on the finding of negative stomach washes in patients arriving with artificial pneumothorax, with pleurisy or having old fibrotic or minimal lesions.

In stage I, 2 patients had both stomach-wash and sputum cultures positive (table IV) and in stage II, 1 patient; 5 patients in stage I who originally were stomach-wash positive but sputum negative, showed a positive sputum some time later, and also 10 stage II patients.

It would seem as if the stomach wash ought to have found bacilli in the 15 patients whose sputum culture showed tubercle bacilli at the same time. Stadnichenko *et al.* (1940) found 100 per cent of such patients positive by the technique they used, but they do not give the standard of sputum examination.

It is possible that the acid method damaged some of the bacilli so that no growth was obtained; other workers too have reported occasional specimens with positive smears and negative cultures; it is also possible that the culture technique is not so sensitive as the animal method; and further the culture technique may need improvement to produce more positives when bacilli are not numerous.

Although the stomach-wash method failed to find tubercle bacilli in every patient diagnosed as suffering from pulmonary tuberculosis by clinical and x-ray examinations, or even in every patient in whom the sputum culture was either immediately or later positive, it is still a valuable aid to diagnosis. On admission 43 out of 213 or 20.2 per cent (table IV) of patients with a series of negative sputum smears were found positive, or, omitting these with a positive sputum culture on admission or a positive sputum later, in 26 of 160 patients (16.3 per cent) tubercle bacilli being found by no other method at any time. The number of patients examined during treatment or on discharge is not very large, but it has proved of some value in the absence of positive sputum smears or cultures in showing that tubercle bacilli are still being eliminated.

Summary

- (1) A short review is given of earlier work on stomach-wash examinations in the West.
- (2) The origin of the tubercle bacilli in the stomach is briefly discussed.
- (3) The present series of 500 patients is reviewed.

(Concluded on opposite page)

THE TECHNIQUE OF THORACOSCOPY AND CAUTERIZATION OF PLEURAL ADHESIONS

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As a treatment for pulmonary tuberculosis, artificial pneumothorax is becoming more and more popular in India. The need for frequent x-ray examinations for the control and maintenance of artificial pneumothorax is also becoming widely recognized. One result of these developments has been the realization of the fact that among those in whom artificial pneumothorax is apparently successful, only a small percentage get a complete collapse of the lung free from pleural adhesions.

For example, among 137 cases of pulmonary tuberculosis treated with artificial pneumothorax in the Lady Linlithgow Sanatorium during the

(Continued from previous page)

(4) A short description is given of the technique.

(5) The results are analysed—

(a) for the whole series according to diagnosis.

(b) for those with pulmonary tuberculosis according to stage of disease and stage of treatment.

(c) for stomach-wash examination compared with sputum examinations.

(6) The findings are discussed, and an examination is made of why some patients even with advanced tuberculosis show a negative stomach wash, and it is concluded that even if this is so, yet in many patients bacilli are found by the stomach wash and by no other method.

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brief period of its existence, only 20 or 14.4 per cent were found under x-ray examination to be free from pleural adhesions. The recognition of this high incidence of pleural adhesions has made the operation of thoracoscopy and cauterization of pleural adhesions to be looked upon as a necessary adjunct to artificial pneumothorax.

The main outline of this operation is described in textbooks on thoracic surgery. The purpose of this article is to add certain practical hints which may be of help to those who are proposing or beginning to do this operation.

Need for x-rays

If x-ray examinations are necessary for the control of artificial pneumothorax, they are absolutely essential before and after thoracoscopy. X-ray really gives us the shadow-view thoracoscope on which to base preliminary knowledge of the rough dispositions inside the chest. This knowledge is necessary before undertaking a thoracoscopy operation.

In such a preliminary x-ray examination, one has to observe the number, position, direction, size, shape, contents, and nature of adhesions, the amount of space available in the pleura, the presence or absence of pleural effusion, the best site for making the first puncture in the chest wall.

In order to get all this information, it will be found necessary to take a series of x-ray photographs in different positions, or to screen the patient at different angles, or to do both. The number, size, shape and contents of pleural adhesions, the amount of pleural space available, etc., may appear different in different positions. The direction of an adhesion is best noted by observing it at different angles to the rays, by turning the patient round under the fluoroscope.

Which adhesions are cauterizable?

Not all adhesions observed are cauterizable. For example, among 106 adhesions thought to be cauterizable by x-ray examination in the Lady Linlithgow Sanatorium, only 87 or 82 per cent were found to be actually cauterizable when seen through the thoracoscope. X-rays give the preliminary impression about cauterizability, but in many cases it is only a direct view through a thoracoscope that can actually determine whether an adhesion is cauterizable or not.

Of course when large areas of a lung are directly adherent to the chest wall, the adhesion cannot be cauterized. If an adhesion is very thick and likely to contain large blood vessels or lung tissue, it cannot be cauterized. Ordinarily it is easy to say where the lung ends and the pleural adhesion begins, because the mottled or marbled appearance of the lung surface is quite different from the uniform white or pink colour of the pleural adhesion. Diseased lung looks dark grey and the surface may be irregular. In cases with much pleural thickening, it is not easy

to see where lung ends and pleural adhesion begins. If a cavity extends right through an adhesion, that adhesion cannot be cauterized. If an adhesion is too close to the large blood vessels of the mediastinum and cannot be lifted off them, it is not safe to cauterize it. String adhesions, however large in number (26 have been observed in a single case in the Lady Linlithgow Sanatorium), can be cauterized. Wide membranous and band adhesions can be cauterized provided that they are thin enough.

According to the distance between the adhesion and the thoracoscope lens, the adhesion may appear magnified or reduced in size. If there is doubt whether the adhesion is being seen in its natural size, the cautery should be placed on the adhesion for comparison. If the cautery tip is seen in its natural size, the adhesion is also being seen in its natural size. Even adhesions shorter than 1 cm. can be severed or dissected off the chest wall, but naturally this is more painful to the patient and more difficult for the operator than the severing of longer adhesions.

Deep penetration skiagrams, transillumination when possible, and a close (magnified) view of the adhesion from different angles will help to determine the contents and nature of adhesions. If rhythmic movements of the adhesions are noticed, it is important to make sure whether the movements are synchronous with respiration or with the pulse. It is also necessary to note whether pulsations are intrinsic or transmitted. When the instrument set includes an anæsthetizing shaft for applying local anæsthesia to the adhesion, it is possible to puncture the adhesion at selected places and observe the result in order to determine whether an adhesion is too vascular for cauterization.

In this operation the determination of the cauterizability of an adhesion is what needs most judgment and experience.

Instruments

Ordinarily the particular instrument to which a surgeon is accustomed will be considered best by him, but when one has used different kinds of instruments, it is possible to form an idea of the comparative merits of different types of instruments. The best known thoracoscopy sets are those designed by Jacobaeus, Chandler, Kremer, Coryllos and Matson.

Instruments may be classified as single- or double-puncture, direct, indirect or parablique vision, straight or curved, flexible or rigid, galvanic or diathermic.

Single- and double-puncture instruments have each their own advantages, but the advantages of the double-puncture type outweigh those of the single-puncture type, and, therefore, if a surgeon proposes to have only one type of instrument, the double-puncture is the one to be preferred.

A single-puncture instrument has the advantages that the patient is saved a second

thoracic puncture, that the thoracoscope and the cautery pass through the same cannula and the cautery tip always remains in view, and it is therefore easier to manipulate inside the chest and to get the light and the cautery on the adhesion at the same time.

When the thoracoscope is introduced into the chest, the lens often becomes cloudy on account of the moisture in the chest, and one has to wait a little before the body heat clears the lens again. In the single-puncture instrument, the lens is close to the cautery tip, and if one can see just enough to be sure that the tip is not touching any structure, the cautery (if galvanic) can be put on, and the heat will at once clear the lens completely. In a double-puncture instrument, this difficulty is often got over by dipping the lens in hot water and drying, or by warming the lens high over a spirit flame before introducing the thoracoscope into the chest. The great disadvantage of a single-puncture instrument is that the adhesion is seen only from one angle and the approach to the adhesion is only from one side.

There is no reason to think that the two smaller punctures needed with a double-puncture instrument are in any way more disadvantageous to the patient than the single but larger puncture required with a single-puncture instrument. There is hardly any shock with either single or double puncture, provided that the skin and pleura are well anæsthetized with plenty of novocain (15 c.cm. of $\frac{1}{2}$ per cent novocain for skin and muscles and 5 c.cm. of 10 per cent novocain for the pleura are not too much for a puncture of a chest wall of average thickness).

The advantages of a double-puncture instrument are: (a) The cautery and light can be interchanged in the two cannulae and then the adhesion can be seen from two different angles. It is often a matter of surprise to operators to see how different the same adhesion looks from different angles. One can go on with the cauterization with much greater confidence when one has seen the adhesion from at least two angles if not all round. (b) The site for the second puncture can be selected at a suitable place after inspecting the adhesion and the general disposition inside the chest through the first puncture. The entrance of the second trocar into the pleural space can be watched through the thoracoscope in the first puncture. With the single-puncture instrument it sometimes happens that when the puncture is made, the adhesion is not easily accessible from that puncture. With the double-puncture instrument, the second puncture can be chosen at a site from which the adhesions will be more accessible. The accessibility of different adhesions can often be improved by interchanging cautery and light in the two cannulae.

The original Jacobaeus instrument was an indirect vision instrument, i.e. the adhesion is seen through a mirror or prism by reflection,

the reflector being placed at an angle to the line of vision. The advantage is that by rotating the shaft of the instrument, a large field can be explored. The disadvantage is that the operator has always to remember that the field he is seeing is not really in the direction of his vision, and that what he is seeing is a reflected image of the object.

In the direct vision instrument, the operator looks directly through a set of lenses at the object in the line of vision. To explore different fields one has to move the lens-shaft in different directions and not merely rotate the shaft in the cannula. Getting the cautery on an adhesion seen by direct vision is naturally easier than when the adhesion is seen by reflection. The latter instruments are all direct vision, and that is to be preferred if only one type of instrument is to be purchased.

The parablique vision thoracoscope (Coryllos) attempts to combine the advantages of the direct and indirect vision instruments. Vision is direct through lenses, but the field you see is at an angle to the line of vision, so that by rotating the handle of the instrument, without changing the direction of the shaft, different fields come into view. In practice this is quite a convenient instrument.

Cautery shafts are straight or curved. The curved ones are designed to facilitate access to awkwardly placed adhesions. With a double-puncture instrument, most adhesions can be reached with straight cauteries. However, it is convenient to have a curved cautery at hand. Cautery tips may be straight or hooked. A hooked tip is of help when adhesions have to be lifted off adjacent structures before being cauterized.

In order to facilitate access to adhesions, cautery shafts which can be bent inside the chest by turning a milled head at the outside end of the cautery shaft have been devised by Matson. This device is ingenious and is useful in exceptional cases, but in the majority of cases, such a refinement is not required.

There has been much controversy regarding the comparative merits of diathermic and galvanic cauteries in severing pleural adhesions. In diathermy, a cold cautery activated by a high frequency current is used. The advantage is that the extent of coagulation of the adhesion can be adjusted to a greater degree than with a galvanic cautery, and thus bleeding can be controlled. In actual practice, if a large blood vessel is opened and there is severe bleeding, coagulation will not help. In all minor bleedings a dull red galvanic cautery will give all the coagulation required. The coagulating capacity of a diathermic cautery depends on the voltage, the amperage and the frequency used, the frequency in turn depending on the spark gap. The relative adjustment of these factors to obtain the desired effect is much more complicated than the change from a red hot galvanic cautery to a dull red cautery by simply reducing the

quantity of current used. If the operator is not thoroughly familiar with the instrument by constant use for a long time, or if the instrument is not well adjusted with regard to voltage, current, and frequency, a diathermic cautery is prone to cut more quickly than you expect, to give unpleasant shocks to the patient, or to fail to coagulate in an emergency when you want it most. Most operators who have experience of both kinds of cautery tend gradually to prefer the galvanic cautery to the diathermic at any rate in the majority of cases. Matson claims that the new Bovie electro-surgical unit is free from the disadvantages of diathermy mentioned above while giving three separate degrees of dehydration.

The operation

Before making the punctures, the light and cautery should be tried to see that they work. The first puncture is made at a side from which the main adhesions will be best visible and accessible as judged by the *x*-rays. This puncture is best selected and marked during the screening in different positions done just before the operation. If the puncture is not far from the mediastinum, care should be taken to direct the trocar inwards and laterally. As far as possible the site of puncture should not be too near the parietal attachment of any adhesion. If the pleural space as seen in the screen is not ample, it is wise to introduce gradually into the pleural space a long needle on a syringe containing a little fluid, withdrawing the piston at every step and thus measure the depth of the space available between the lung and the chest wall at the selected site.

The inside of the chest is surveyed through the first puncture and a site for the second puncture is selected according to the general disposition of the lung and adhesions as seen by direct vision, and the entrance of the second trocar is watched through the first puncture. The second puncture should not be too near the first, as otherwise the light and the cautery will go in more or less parallel to each other and then the view of the cautery will be distorted and unsatisfactory. The aim should be to select the second puncture at a site from which the adhesions will be accessible but not too near to them. The cautery when placed on the adhesion should be as far as possible at right angles to the line of vision through the other puncture.

The adhesions should invariably be examined through both punctures before cauterization is done.

Blood from the puncture trickling down the cannula on to the lens at the distal end of the thoracoscope will make the field of vision look blood-red. One is apt to be frightened by this, thinking that one is looking into a pool of blood inside the chest. It is a good practice to clean the cannula of all blood from the puncture, before the thoracoscope is introduced. Except when an adhesion is evidently detached from all

surrounding structures, it is best to have the cautery under the adhesion lifting it up and thus making sure that the under side of the adhesion is not attached to or is in contact with some vital structure. Large adhesions should be cauterized slowly step by step. Adhesions left partly cauterized tend to stretch and can often be tackled more easily at a later sitting. Before closing the punctures it is wise to have a look at all stumps to make sure that there is no bleeding.

Post-operative treatment

Where there has been no bleeding during the operation, it is a wise practice to screen the patient before returning him to bed. The amount of air left in the pleural space after a thoracoscopy varies very much in different cases. In some, much more air than before the operation will be found, and in others, much less. In no case should a fluoroscopy examination be put off for many days after a thoracoscopy. If this is done, one runs the risk of finding the lung much more adherent than before the operation. The need for early and frequent fluoroscopy examinations during the post-operative period cannot be over emphasized. These are necessary to judge the degree of success of the operation, to keep watch on the pleural effusion that may appear, and above all to adjust the pneumothorax and prevent its obliteration.

The patients should be warned about the possibility of surgical emphysema, so that they may not be unnecessarily alarmed about it. A few doses of 20 minims of liq. morphia or $\frac{1}{2}$ gr. of codeine during the immediate post-operative period will allay cough and thus minimize subcutaneous emphysema. The nurse should be instructed to watch for signs of secondary internal hæmorrhage, such as a quick thready pulse, excessive thirst, pallor of the face, etc.

Summary

1. Some practical hints are given for those who are proposing to undertake the operation of internal pneumolysis.
2. The relative merits of the different types of instruments are discussed.
3. The need for x-ray control of the operation and post-operative treatment is emphasized.

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PLEURAL EFFUSION IN ARTIFICIAL PNEUMOTHORAX: ITS INCIDENCE IN CASES TREATED FROM THE BEGINNING IN AN OUT-PATIENT DEPARTMENT*

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PLEURAL effusion in cases treated with artificial pneumothorax demands consideration both for its good and evil effects. Some of its good effects are: the fixation of the mobile mediastinum thus affording better collapse, the closure of the basal cavity, the increase of interval between the fills by better retention of gas, and the initiation of better fibrosis by 'auto-tuberculin reaction'. None of these, of course, is an unmixed good, but even if we accept them as good effects, the obvious evil effects are much more prominent. Among the evil effects, empyema formation is most serious but oblitative pleurisy is most frequent. Other ill effects are the difficulty in the re-expansion of the lung, the shortening and thickening of adhesions resulting in re-opening of the cavity, the chance of collapse becoming contra-selective (most of the lesions are in the upper zones, while effusion collapses the lower zone more), the occurrence of certain unpleasant gastric symptoms especially in left side cases, and toxic symptoms associated with effusion. It is true that a majority of such effusions get absorbed quickly without doing any ultimate harm, but many cases are left to suffer. That the problem of effusion is important is clearly shown by a very large number of publications on the subject from all countries.

Literature available to us shows that the studies were made mostly in patients in sanatoria or institutions. In them, at least for the initial period of a couple of months, the therapy is conducted with the patient in bed. The conduct of treatment from its very commencement in an out-patient department, as we have done it, implies movement on the part of the patients. In most instances, this movement has been considerable. It is generally considered that movement during the early part of treatment favours effusion formation. It is, therefore,

*The article was originally accompanied by 11 large tables giving the findings of this study in full. At the request of the Editor the number of tables has been reduced in order to save space.

expected that this risk should be more in our series of patients. To assess the risk of effusion formation in such particular circumstances is the object of this paper.

As the number of beds for tuberculosis cases is very insufficient in every province of India, such ambulatory conduct of artificial pneumothorax treatment might be a necessity elsewhere also. The assessment of this risk, therefore, is likely to be specially useful in such circumstances.

The cases recorded here represent a cross section of the type of population which visits clinics. These persons are generally poor and mostly uneducated. They generally have nothing to fall back upon during the time of distress, and have less rest, both of body and of mind, than the type of person who can afford sanatorium treatment. For the above reasons, and for lack of direct control over the cases of an out-patient department, many of the cases in this series did not complete the course of treatment. This was the inherent difficulty in studying such a series. As this difficulty is likely to be present in all such clinic groups, and as it is necessary to get a complete view regarding the incidence of effusion in such a community, the whole group has been accepted for study. This will provide us with information as to what is likely to happen in cases having artificial pneumothorax treatment in an out-patient department.

It is common knowledge that the detection of the presence of small effusions requires frequent and careful radiological study. Therefore, the incidence will largely depend on the opportunity available and the care given to this study. We took special care to detect small effusions by bringing the x-ray tube and the level of the fluid in the same plane. It was the general rule during artificial pneumothorax treatment at our clinic to have a skiagram made in the first month and thereafter at three-monthly intervals. Screening was done more frequently whenever anything warranted it. All these examinations were made in the Radiology Department of the College prior to 1939. Since 1939 the Chest Department has had its own screening outfit, and screening was more frequent, usually at about fortnightly intervals, or even more frequently if anything suggested it. Thus it is likely that the accuracy with which effusion was detected might differ for the periods before and since 1939. If a significant difference in these rates exists, then the series should be divided all through into two groups relating to the above-mentioned periods. From the earlier period 378, and from the later-period 122, cases were accepted. Among the 378, 180 or 48 per cent, and among the 122, 58 or 47 per cent developed effusion. Such comparisons are likely to be erroneous without allowance for other factors which are likely to have a significant effect on effusion formation. Tables with such allowances were made. These also

did not show any significant difference in the rates of the two periods. Therefore, all the 500 cases could be treated in one group.

Risk of effusion

In this series of 500 cases under artificial pneumothorax treatment, 238 or 47.6 per cent showed the presence of effusion in the pleural space some time during the course of treatment.

De Cecio and Potter (1939) found effusion in 34 per cent of their 595 cases. The incidence of effusion in the 375 cases of Nicklas *et al.* (1937) was 67.5 per cent, in Weisman's (1936) 150 cases 84.0 per cent, in Burrell's (1926) 151 cases 82.8 per cent. It is not necessary to quote more figures. The above clearly show how greatly the rate may vary with different workers. On an average, the variation recorded in all the available literature was from 50 to 80 per cent.

The causes for such wide variations may be many, but it is well known and all the previous studies have shown that the longer one continues artificial pneumothorax treatment, the greater is the chance of getting effusion or, in other words, the risk of effusion varies with the duration of treatment. This is not difficult to understand. A man undergoing artificial pneumothorax treatment runs a certain risk of effusion during the first month. If he escapes it in the first month he experiences a further risk in the second month and so on. Hence with longer duration of treatment, the greater is the risk of effusion.

For this reason, a comparison based on mere incidence figures is of little value, since the period of treatment varies markedly. What can be considered of importance is the study of how the chances of getting effusion vary with the length of treatment. One method of studying this question is as follows.

All the cases will continue treatment for a certain period. In our series the minimum is six weeks. Of these some will get effusion. The proportion of cases showing effusion in this period gives the risk for this period.

After this period some will discontinue treatment and others will continue. Of those that continue, only those that covered a second period fully will be accepted. Among these, some have had an effusion in the first period and these also will be excluded and the risk is calculated on the remainder; similarly for the later periods.

After working out the risks for various periods in this manner it is possible to integrate them into a curve showing how many in 100 persons starting treatment at the same time and continuing it for the same length of time, would be without effusion after a specified length of treatment.

In this method it is assumed that if the non-effusion cases who left off treatment early had continued it, their risk to subsequent effusion would be fully reflected by the risk experienced by those who had the treatment for a longer time.

For drawing this integrated curve it is necessary to know whether or not the incidence of effusion in any particular period (in this case 'month') is, on an average, the same for all persons who had treatment up to that time or more. For example, the incidence of effusion in the second month in the cases that had 3 to 6 months' treatment might differ from those that had 6 to 9 months or longer period of treatment. Unless this rate of effusion in any specified period is

not significantly different in different groups with different duration of treatment, an integrated curve from a pooled estimate of risk from all cases will not be justified.

In this series the duration of treatment of the 500 cases has been shown in table I as up to 3 months, up to 6 months, etc., in relation to effusion and non-effusion cases. The time of appearance of effusion has been noted as within one month, within 2 months, etc.

Incidence of effusion in the first month in all the groups with different duration of treatment.—

In the '3 months group' of 127 cases, 41 or 32.3 per cent developed effusion. This percentage does not represent complete risk for the first 3 months as all the cases did not cover full 3 months. But, as no case has been accepted at less than 6 weeks' treatment, and as the time of effusion has been given as less than one month, less than 2 months, etc., the incidence for the first month can certainly be determined.

Twenty-nine, or 22.8 per cent, had effusion in the first month. In the 3 to 6 months group of 133 cases, 9 or 6.8 per cent showed effusion in the first month. In those who had longer durations of treatment the proportion of effusion in the first month was 6 to 72 or 8.3 per cent, 5 to 47 or 10.6 per cent, 4 to 69 or 5.8 per cent and 2 to 52 or 3.8 per cent. Though in percentages

having treatment for different durations are few and small differences are likely to be missed. Statistical analysis does not show significant variations in risk for any one specified period.

The above analysis leads to the following result: that the risk of effusion for any specified period did not vary for different groups with different durations of treatment except in those who had treatment for less than 3 months. Therefore it appears justifiable to assume that the risk for any specified period is in general the same for all groups with varying durations of treatment and it would be reasonable to estimate the risk for a specified period by considering all the groups pooled together irrespective of the total duration of treatment.

The risk in the first month is given by 55 cases of effusion out of 500 or 11 per cent. For risk in the second month the number exposed is $(124 + 66 + 42 + 65 + 50) = 347$ and the number of cases of effusion $(14 + 10 + 7 + 6 + 13) = 50$ giving the risk as 0.1441. This shows that out of 100 cases without effusion in the first month, 14.4 will in the long run develop effusion within the next one month. Similarly the risk in the third month is 29 out of 297 cases or 9.8 per cent.

TABLE I

Showing the duration of treatment and the incidence of effusion

Duration of treatment	TIME OF EFFUSION										Total effusion	Total cases
	-1 m.	-2 m.	-3 m.	-4 m.	-5 m.	-6 m.	-1 yr.	-1½ yrs.	-2 yrs.	Over 2 yrs.		
-3 months ..	29	7	5	41	127
-6 " ..	9	14	11	12	3	49	133
-9 " ..	6	10	9	5	5	4	3	42	72
-1 year ..	5	7	2	1	1	3	9	28	47
-1½ years ..	4	6	7	5	3	3	8	3	39	69
Over 1½ years ..	2	13	..	2	4	..	11	3	2	2	39	52
TOTAL ..	55	57	34	25	16	10	31	6	2	2	238	500

the groups show variation, on statistical analysis by 'Chi-square' test these differences are not found significant except in the case of the group with less than 3 months' treatment.

Incidence of effusion in the second month and later months among the groups with different duration of treatment.—This incidence is determined from the groups with 3 to 6 months' treatment and more, as all of them must have covered the second month of treatment.

In the '3 to 6 months group' of 124 cases who were without effusion at the end of the first month, 14 or 11.3 per cent developed effusion in the second month. In other groups the proportion of effusion was 10 to 66, 7 to 42, 6 to 65 and 13 to 50. These proportions are not significantly different.

For the third month the risk is shown by 11 out of 110 for those who had treatment for 3 to 6 months and for other groups 9 out of 56, 2 out of 35, 7 out of 59 and nil out of 37. These proportions are not significantly different.

For the fourth month and for longer duration of treatment the numbers showing the risk in each group

From the determination of the risk at various periods it is possible to work out the number of non-effusion cases at different times amongst a group of 100 persons all starting their course of treatment at the same time and continuing it for the same length of time. The method to be applied can be seen from the application to the first 2 months.

At the end of the first month 89 persons will be without effusion. As the risk in the second month is 0.1441, the number of effusion cases during this period from the 89 cases would be $89 \times 0.1441 = 12.8$. So 76.2 persons will be without effusion at the end of the second month. The numbers for longer durations are shown in table II and a graphical representation is made (see graph).

Out of 100 cases 11 get effusion within a month, a further 13 within the next month, about 7 to 8 more cases in the third month and so on, with the result that at the end of 1½ years only 34 would not have developed effusion. The risk of effusion is much more in the beginning as can be seen from the steep decline of the curve during the first few months.

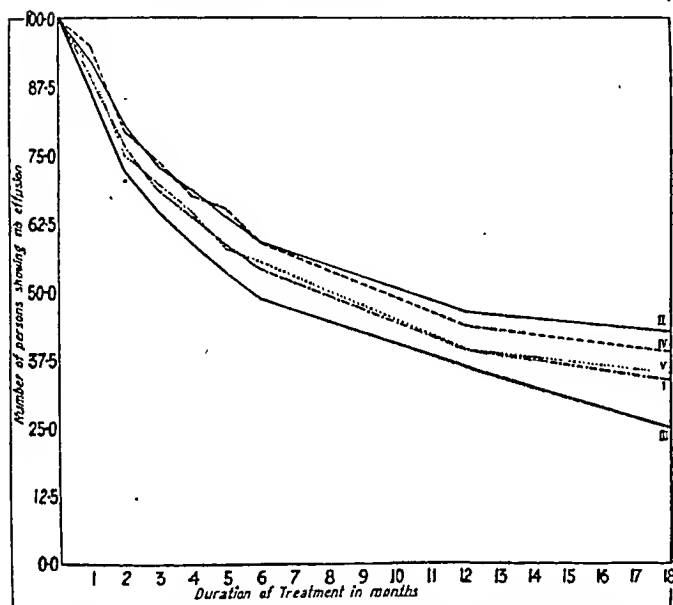
On the limitation of the applicability of the curve the following comments may be made :—

(1) The 500 cases were taken as they came to the out-patients department and there is every possibility of a selection of cases in favour of or against one or more factors. The figure in the text (*see graph*) refers only to a community from which the 500 can be considered a random sample.

GRAPH

Showing the number of persons out of 100 who do not develop effusion within any specified duration of treatment.

- I. Risk estimated from all the data.
- II. Lower limit for risk (all data).
- III. Upper limit for risk (all data).
- IV. Risk estimated from cases with over 18 months' treatment.
- V. Risk estimated from cases with over 18 months' treatment (corrected).



(2) The numbers on which the risks are calculated are rather small for periods over 6 months and therefore less reliable. The upper and lower limits given in table II and also marked on the curve serve, however, to mitigate the uncertainty. It is of interest to compare the rate of effusion as worked out from the whole data with that experienced by those individuals who had treatment for at least 1½ years.

Table I shows that 121 individuals belonged to this group and of them 6 get effusion within a month of

treatment, 25 within 2 months of treatment, 32 within 3 months of treatment and so on. In all 74 had effusion before 1½ years. This risk is given in table II and is represented in the figure (*see graph*) by the number of non-effusion cases at any time out of 100 individuals all starting their treatment together. This risk coincides with the lower limit for the risk as obtained from the pooled data. The smaller risk for this selected group is not surprising as it has already been shown that the individuals who continued treatment longer than 3 months experienced less risk within a month than those who did not. If this difference is allowed for, at least 5 more cases of effusion within first month could be reasonably expected amongst the 121 individuals. The corrected risk with this adjustment is also shown in table II and in the figure (*see graph*) and the corrected risk compares very favourably with the general risk already worked out.

Some factors influencing effusion

It has already been remarked that the longer the duration of treatment, the greater is the incidence of effusion. Therefore the assessment of the effect of factors should not be carried out by a direct comparison of the percentage of effusion under the various heads (say stage I, stage II and stage III) of the factor (extent of disease) as this will not allow for any differences in the duration of treatment between the different stages. If the rate of effusion for any specified period is not affected by the total duration of the treatment, and if the relative proportion of individuals for each duration of treatment is the same for all heads of the factor, such a direct comparison is permissible. Even if these conditions are satisfied, it is preferable to use another method. In this method, the risk for various periods is worked out in the manner described already for each factor, and the risks for various periods are compared. This method has the advantage of bringing out possible variations in the risks at each period and is, therefore, more sensitive.

The factors considered are : (1) sex, (2) age, (3) habitation, (4) the stage of disease, (5) the character of disease, (6) the nature of collapse, (7) the presence or absence of adhesions and (8) the mobility of mediastinum. Factors such as pleural pressure, situation of the lesions, toxic

TABLE II

Showing the number of cases out of 100 not developing effusion within a specified duration of treatment

Duration of treatment	Estimate from all data	Lower limit for risk (all data)	Upper limit for risk (all data)	Estimate from cases with over 18 months' treatment	Corrected estimate from cases with over 18 months' treatment
At start ..	100.0	100.0	100.0	100.0	100.0
1 month ..	89.0	91.8	86.2	95.0	90.9
2 months ..	76.2	80.4	72.0	79.3	75.2
3 " ..	68.7	73.2	64.3	73.6	69.4
4 " ..	63.5	68.3	58.6	67.8	63.7
5 " ..	58.2	63.4	53.0	62.0	57.9
6 " ..	54.1	59.5	48.7	59.5	55.4
12 " ..	39.8	46.7	32.9	43.8	39.7
18 " ..	33.9	42.5	25.2	38.8	34.7

condition of the patient, etc., are not included in this study.

(1) *Sex*.—Four hundred and three patients were males, and only 97 females. The risk at all periods were the same for both sexes.

months; of the other 2, one had treatment for less than 3 months and the other for less than one year. There is a suggestion that the incidence is high in earlier years. In the other three groups the risk is almost the same.

TABLE III

Showing the duration of treatment and the incidence of effusion according to stage of disease

Duration of treatment	STAGE I											
	Time of effusion											
	-1 m.	-2 m.	-3 m.	-4 m.	-5 m.	-6 m.	-1 yr.	-1½ yrs.	-2 yrs.	2 + yrs.	Total effusion	Total cases
-3 months	1	1	3
-6 "	1	1	8
-9 "	1	1	1
-1 year	1	1	1	3	3
-1½ years	1	1	..	1	1	4	8
-1½ + years	2	..	1	1	4	4
TOTAL	4	1	3	1	1	2	2	14	27

Duration of treatment	STAGE II											
	Time of effusion											
	-1 m.	-2 m.	-3 m.	-4 m.	-5 m.	-6 m.	-1 yr.	-1½ yrs.	-2 yrs.	2 + yrs.	Total effusion	Total cases
-3 months ..	7	..	2	9	22
-6 "	1	2	1	1	5	14
-9 "	3	3	1	..	1	1	9	18
-1 year ..	1	1	2	4	8
-1½ years ..	1	..	1	3	1	1	2	9	14
-1½ + years	2	..	1	3	..	4	10	14
TOTAL ..	9	6	8	6	5	3	9	46	90

Duration of treatment	STAGE III											
	Time of effusion											
	-1 m.	-2 m.	-3 m.	-4 m.	-5 m.	-6 m.	-1 yr.	-1½ yrs.	-2 yrs.	2 + yrs.	Total effusion	Total cases
-3 months ..	22	6	3	31	102
-6 " ..	9	13	9	10	2	43	111
-9 " ..	6	7	5	4	5	3	2	32	53
-1 year ..	4	6	2	1	1	1	6	21	36
-1½ years ..	3	6	6	1	1	2	5	2	26	47
-1½ + years ..	2	9	1	..	7	2	2	2	25	34
TOTAL ..	46	47	25	16	10	6	20	4	2	2	178	383

(2) *Age*.—Seven patients were between 5 and 14 years, 190 between 15 and 24 years, 256 between 25 and 39 years and the other 47 over 40 years. Observations below 14 years were too few, yet out of the 7, 5 showed effusion within 3

(3) *Habitation*.—Three hundred and fifty-one patients had an urban habitat, 73 semi-rural and 76 rural. In general the habitat did not affect the risk of effusion but there is a definite indication that the risk within a month is less

for individuals with a rural habitation. This difference results mainly from differences in the incidence of effusion amongst those who had treatment for less than 3 months. Out of 84 with an urban habitat, 21 had effusion in the first month; out of the 21 with semi-rural habitat, 7 had effusion in the same time; while amongst the 22 with a rural habitat only one had effusion in the first month. The risk of effusion within a month is found to be much less in those who came from a rural setting.

necessary in severe diseases, remains a pertinent question.

(5) *The character of disease (table IV).*—For 4 out of the 500 cases dealt with, the character of the disease was not recorded. Of the rest, 372 were of exudative type, 123 were of intermediate type and one was of productive type. Analysis did not bring out any difference in the risk to effusion with the character of the lesions. The number of productive lesions is insignificant, and cannot be taken into account.

TABLE IV

Showing the duration of treatment and the incidence of effusion according to character of disease

Duration of treatment	EXUDATIVE TYPE											
	Time of effusion											Total cases
	-1 m.	-2 m.	-3 m.	-4 m.	-5 m.	-6 m.	-1 yr.	-1½ yrs.	-2 yrs.	2 + yrs.	Total effusion	
-3 months ..	20	4	5	29	93
-6 " ..	4	11	8	11	3	37	96
-9 " ..	5	8	8	1	5	3	2	32	55
-1 year ..	4	5	2	1	..	2	6	20	32
-1½ years ..	3	3	6	5	2	2	5	2	28	53
1½ + years ..	2	8	..	2	4	..	11	3	2	1	33	43
TOTAL ..	38	39	29	20	14	7	24	5	2	1	179	372

Duration of treatment	INTERMEDIATE TYPE											
	Time of effusion											Total cases
	-1 m.	-2 m.	-3 m.	-4 m.	-5 m.	-6 m.	-1 yr.	-1½ yrs.	-2 yrs.	2 + yrs.	Total effusion	
-3 months ..	9	2	11	32
-6 " ..	5	3	3	1	12	36
-9 " ..	1	2	1	4	..	1	1	10	16
-1 year ..	1	2	1	1	3	8	15
-1½ years ..	1	3	1	..	1	1	3	1	11	15
1½ + years	5	1	6	9
TOTAL ..	17	17	5	5	2	3	7	1	..	1	58	123

(4) *The stage of disease (table III).*—Twenty-seven cases were in stage I, 90 in stage II and 383 in stage III. A slightly higher proportion of cases of effusion in the first and second months was noticed in stage III compared with stage II, but the difference was not significant. Packard *et al.* (1940) are of the opinion that, with the severity of the disease, the effusion rate increases. He cites observations from Saranac Lake and Trudeau Sanatorium. Eng (1940) also gives the rate as 33.3 per cent in minimal, 56.3 per cent in moderately advanced and 78 per cent in far advanced cases. Whether such an increased rate is due to severity of the disease or due to longer duration of treatment, as is generally

(6) *The nature of collapse.*—One hundred and fifty-one cases had effective collapse, 74 ineffective and 275 partial collapse. The risk of effusion did not vary with the nature of collapse.

(7) *The presence or absence of adhesion (table V).*—Four hundred and eleven cases showed adhesion and 89 were without them. No relationship of risk to effusion with the presence or absence of adhesions emerged.

(8) *The mobility of the mediastinum.*—Of the 500 cases, 456 had an almost fixed mediastinum. The number with a mobile mediastinum was too small to bring out small differences. Statistical analysis does not reveal

any difference in risk with differences in the mobility of the mediastinum.

The relationship of the amount of effusion to the time (commencement) of effusion.—Effusions were classified in three groups : (1) slight : when the level of effusion just filled the costophrenic angle on standing; (2) moderate : more than above, till the level of the fluid reached up to the top of the diaphragm; (3) massive : more than (2). We made no attempt to classify the effusion into simple and purulent, as there is

effusion is not in any way related to the time of commencement of effusion. The proportion of slight to moderate effusion is in the ratio of 3 to 2 approximately.

Summary

Five hundred cases treated with artificial pneumothorax have been studied with reference to the incidence of pleural effusion.

It has been stressed that as the duration of treatment has a definite effect on the incidence,

TABLE V

Showing the duration of treatment and the incidence of effusion with adhesion and without adhesion

Duration of treatment	ADHESION											
	Time of effusion											Total cases
	-1 m.	-2 m.	-3 m.	-4 m.	-5 m.	-6 m.	-1 yr.	-1½ yrs.	-2 yrs.	2 + yrs.	Total effusion	
-3 months	24	5	4	33	107
-6 "	7	12	9	10	3	41	114
-9 "	6	9	5	4	5	3	3	35	58
-1 year	3	6	1	1	1	1	7	20	36
-1½ years	4	6	5	5	2	2	8	3	35	60
1½ + years	2	9	..	1	2	..	8	1	2	2	27	36
TOTAL	46	47	24	21	13	6	26	4	2	2	191	411

Duration of treatment	WITHOUT ADHESION											
	Time of effusion											Total cases
	-1 m.	-2 m.	-3 m.	-4 m.	-5 m.	-6 m.	-1 yr.	-1½ yrs.	-2 yrs.	2 + yrs.	Total effusion	
-3 months	5	2	1	8	20
-6 "	2	2	2	2	8	19
-9 "	..	1	4	1	..	1	7	14
-1 year	2	1	1	2	2	8	11
-1½ years	2	..	1	1	4	9
1½ + years	..	4	..	1	2	..	3	2	12	16
TOTAL	9	10	10	4	3	4	5	2	47	89

difference of opinion as to when an effusion should be called purulent. No reference will, therefore, be made to the incidence of empyema, etc., in this paper.

Of the 238 effusions, 133 were slight, 97 moderate, 6 massive. (In 2 cases, records regarding the amount were missing.) The two former groups are shown in table VI according to the time of effusion and the duration of treatment. In the slight and moderate cases, out of 53 cases of effusion within a month 33 were slight. Of the 49 cases of effusion in the second month (considering only cases which were definitely at risk) 30 were slight. Similarly of the 28 in the third month 14 were slight. Of the 13 in the fourth month 5 were slight. Of another 13 in the fifth month 8 were slight, and of the 10 in the sixth month 7 were slight. The proportion of slight to moderate is not statistically different in the different periods; thus the amount of

and as this duration is likely to vary from one study to another, a direct comparison on total incidence figure is not justified.

For the above reason, a curve showing the risk of effusion at different periods in the course of treatment has been worked out. This shows that out of 100 persons having artificial pneumothorax treatment 11 will develop effusion in the first month. Of the rest, 13 will develop effusion in the second month. Of the rest, 7 or 8 will develop effusion in the next month and so on, with the result that after 18 months' treatment only 34 will not have developed an effusion. The curve indicates that the rate is higher in the earlier months.

TABLE VI

Showing the duration of treatment and the amount of effusion

Duration of treatment	SLIGHT										
	Time of effusion										
	-1 m.	-2 m.	-3 m.	-4 m.	-5 m.	-6 m.	-1 yr.	-1½ yrs.	-2 yrs.	2 + yrs.	Total
-3 months ..	18	1	3	22
-6 " ..	4	8	5	6	2	25
-9 " ..	3	8	6	2	2	3	1	25
-1 year ..	4	3	..	1	1	2	5	16
-1½ years ..	3	6	3	..	2	2	5	2	23
1½ + years ..	1	5	..	2	3	..	7	2	1	1	22
TOTAL ..	33	31	17	11	10	7	18	4	1	1	133

Duration of treatment	MODERATE										
	Time of effusion										
	-1 m.	-2 m.	-3 m.	-4 m.	-5 m.	-6 m.	-1 yr.	-1½ yrs.	-2 yrs.	2 + yrs.	Total
-3 months ..	10	6	2	18
-6 " ..	4	6	5	6	1	22
-9 " ..	3	2	3	3	3	1	1	16
-1 year ..	1	4	2	1	4	12
-1½ years ..	1	..	4	5	1	1	3	1	16
1½ + years ..	1	7	1	..	2	..	1	1	13
TOTAL ..	20	25	16	14	6	3	10	1	1	1	97

The influence of factors—sex, age, habitation, stage of disease, character of disease, nature of collapse, presence or absence of adhesions and mobility of mediastinum—has been assessed, taking the duration of treatment into consideration in each case. None of these factors showed any significant effect on the formation of effusion. There is only a suggestion that in childhood the rate is higher, and people of rural habit show a slightly lower rate in the first month.

No relationship could be detected between the amount of effusion and the time of its commencement. The proportion of slight to moderate amount of effusion is found to be 3 to 2. The number with massive effusion is few.

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INTESTINAL TUBERCULOSIS : ITS DIAGNOSIS AND SIGNIFICANCE IN THE TREATMENT OF PULMONARY TUBERCULOSIS

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THE interest in intestinal tuberculosis has increased steadily since the publication in 1926 of Brown and Sampson's book on the diagnosis and treatment of this common complication in pulmonary tuberculosis. Though they were not the first to demonstrate the typical x-ray findings in intestinal tuberculosis, they certainly deserve credit for having put x-ray diagnosis on a rational basis. They showed convincingly that this method was definitely superior to any other

method of diagnosis, both in its reliability and in making an early diagnosis possible where other means failed. Their insistence upon the beneficial effect of heliotherapy in intestinal complications of tuberculosis stimulated further work though at the same time arousing a lively controversy.

In the Union Mission Tuberculosis Sanatorium at Arogyavaram this method of diagnosing intestinal tuberculosis has been in constant use since 1932, but in the earlier years was applied only to specially suspected cases. In this paper is presented an analysis of a series of 163 patients examined within the last one and a half years by the author; the earlier examinations were based mostly on fluoroscopic findings only and no x-ray films were available for the present study. The purpose of the present investigation was, first, to determine the incidence of intestinal tuberculosis among the patients in the sanatorium, second, to see if any light could be thrown on the question of the aetiology of intestinal tuberculosis in Indian patients, and third, to find out how close was the agreement between the radiological and the clinical diagnosis based upon symptoms generally considered characteristic.

X-ray diagnosis of intestinal tuberculosis

The radiological method of diagnosing tuberculous processes in the intestine is based upon two main observations. First, the earliest and most commonly affected area of the digestive tract is the distal part of the ileum, the caecum and the ascending colon. Fenwick and Dodwell (1892) in 500 autopsy cases of tuberculosis found the ileum and caecum affected in 85 per cent, Schwatt and Steinbach (1923) the ileum in 84 and the caecum in 67 per cent of 199 cases, Goldberg, Sweany and Brown (1928) the ileum in 83 and the caecum in 87 per cent of 230 cases, and Tisell (1938) the ileum and the colic valve in 87 per cent, the caecum in 81 and ascending colon in 74 per cent of 61 cases. Among 203 Indian patients with intestinal tuberculosis, Tribedi and Gupta (1941) found post mortem the ileum involved in 86.7 per cent and the ileo-caecal region in 65 per cent. From this brief survey it is evident that only in a small percentage of cases of intestinal tuberculosis do the ileum and the caecum escape involvement. It is therefore most profitable to pay particular attention to these regions when attempting to demonstrate intestinal tuberculosis by the x-ray method.

Secondly, it has been shown that a tuberculous lesion in the ileum or caecum causes very characteristic changes in the x-ray picture so that a diagnosis can be made with a high degree of certainty. This is borne out from investigations in which an x-ray diagnosis could be checked in the same patient either by operation or by autopsy.

Brown and Sampson (1930) report on 180 x-ray examinations of which 122 were checked by operation and 58 by autopsy. Of the 'operated' group, 49 of 54 x-ray positive cases were confirmed, mostly by an exploratory laparotomy; of the five cases proved to be non-tuberculous, four had no pulmonary tuberculosis either. Of 68 x-ray negative cases five showed on operation evidence of abdominal tuberculosis; three had chronic tuberculous appendicitis, one tuberculous salpingitis and peritonitis, and one had extensive tuberculous enteritis and colitis. It detracts from the value of the investigation that in 18 of 80 cases operated on for which data are available, the interval between x-ray examination and operation varies from one to eight years, in three of these the operation preceding the x-ray examination.

Since Brown and Sampson's cases checked by autopsy were in 45 instances examined by Gardner (Brown and Sampson, 1930) and included in his material of 95, they require no special comment. Gardner's results were as follows:—

X-ray diagnosis	POST-MORTEM FINDINGS		
	Number examined	Cases with intestinal tuberculosis	
		Number	Percentage
Positive ..	58	57	98.3
Negative ..	37	18	48.7

The one x-ray positive case not directly confirmed by autopsy showed severe amyloidosis. The 18 x-ray negative cases found positive, presented mainly small, acute ulcers which Gardner considered could very well have arisen during the period following the x-ray examination; some of the ulcers were situated in the ileum only.

Steinbach (1930) found a positive x-ray diagnosis confirmed in 20 out of 27 post-mortem cases, whereas he found agreement in only 7 out of 25 x-ray negative cases, the remaining showing tuberculous lesions.

Tisell (1938) in a beautifully illustrated monograph gives a detailed report on 178 tuberculous patients all examined with a barium meal. Sixty-one of these were examined by autopsy as seen from the following table:—

X-ray diagnosis	Number examined	Number checked by autopsy	Percentage
Positive ..	80	49	61.3
Negative ..	98	12	12.3

It should be noted that whereas nearly two-thirds of the x-ray positive cases could be checked by a post-mortem examination the correctness of a negative x-ray diagnosis could not be checked in the great majority of cases. This is typical for all similar investigations, and it means a great handicap in evaluating the efficacy of the x-ray method. Since most of the x-ray negative cases which come for autopsy come because the patients have died from a progressive pulmonary tuberculosis, it is not unnatural to find at autopsy that a fairly high percentage have developed intestinal tuberculosis. This was also seen by Tisell who found in his 61 post-mortem cases the following results:—

X-ray diagnosis	POST-MORTEM FINDINGS		
	Number of cases	Cases with intestinal tuberculosis	
		Number	Percentage
Positive ..	48	48	100
Negative ..	12	6	50
Doubtful ..	1	0	..

The conclusion to be drawn from this short review is that the x-ray method of demonstrating intestinal tuberculosis in patients with

pulmonary tuberculosis rarely fails with regard to the accuracy of a positive diagnosis but a negative diagnosis does not wholly exclude the possibility of intestinal tuberculosis.

Typical x-ray findings

(a) *Filling defects.*—Of paramount importance for the diagnosis of tuberculosis of the cæcum and ascending colon is the demonstration of permanent irregularities and defects in the barium shadow together with a narrowing of the lumen of the bowel. In its extreme form, the lumen becomes so constricted that no barium or only a very thin 'string-like' shadow can be seen, although barium is found on either side of the affected area; this sign is named after Stierlin who pointed it out as early as 1911. Since the narrowing of the lumen is due mainly to a muscular spasm of the intestine, Gram and Möller (1929) have proposed for it the term 'spastic filling defect'. Good descriptions are given by Brown and Sampson (1930), Gram and Möller (1929) and by Tisell (1938).

Tisell, making use of the experience and technique evolved from Forsell's clinic known for its pioneer work on the radiology of the digestive tract, compared the x-ray picture *in vivo* with that obtained *post mortem* by photographing ileum-colon specimens filled with opaque emulsion. By fixing the body by intra-arterial injections of formalin as soon after death as possible, he was able to preserve intact the fold formation of the mucous membrane which other-

cause marked fold formation of the adjacent mucous membrane by contraction of the muscularis mucosa, in addition to congestion and œdema of the submucosa. As was demonstrated by Akerlund in duodenal ulcers, these folds may assume such proportions that they completely cover up and protect the ulcerations which only communicate with the intestinal lumen through a pin-hole channel. When many ulcerations are present, situated close to each other, the whole wall of the intestine becomes very irregular, and the shadow of the barium lying in the intestine presents a nibbled or ragged outline. Where the barium dips in between the folds or into the channels leading down to the ulcers (the receptacula in Tisell's drawing) needle-like, pointed excrescences may be seen. If the barium column is not too massive, the outline of the folds may also be seen through the main shadow. An example of Tisell's technique is given in the autopsy case reported at the end of this paper (figures 2 to 4, plates XXV and XXVI).

From Tisell's work it is easy to understand how it may be possible to demonstrate the presence of only a few ulcerations or even a single ulcer. The outline of the mucosa shown by the barium shadow is usually much more irregular than would correspond to the ulcer itself. What is seen on x-ray is not the shadow of the actual ulcer but the shadow of the fold formations caused by it.

Another feature of interest is a semilunar appearance produced by an involvement of the labiæ of the colic valve; the valve may become swollen and thick and often protrudes into the cæcum with an appearance resembling cervix uteri (figure 6, plate XXVI). This sign was described by Fleischner (1928).

(b) *Abnormal motility.*—Another finding generally considered of significance for the diagnosis is either hypermotility as evidenced by an acceleration of the passage of the barium through the colon, or a retardation as shown by an ileal stasis. Brown and Sampson consider an empty cæcum at the 24 hours' examination as the most important sign of hypermotility. It is, however, apparent from their series of patients checked by operation or autopsy that they consider filling defect superior to hypermotility for a diagnosis of intestinal tuberculosis. Of their 180 cases, details with regard to the 24 hours' evacuation of the cæcum are given in 172; 85 cases showing filling defect were classified as x-ray positive although in 11, or 12.9 per cent, the cæcum still contained barium while 87 cases without filling defect were classified as x-ray negative although in 9, or 10.3 per cent, the cæcum was empty.

An ileal stasis is considered pathological by the same authors when the barium has not entered the cæcum 6 hours after ingestion of the meal; so is retention of the barium in the ileum after a period of 8 to 9 hours. Ileal stasis points to an involvement of the terminal ileum or the colic valve.

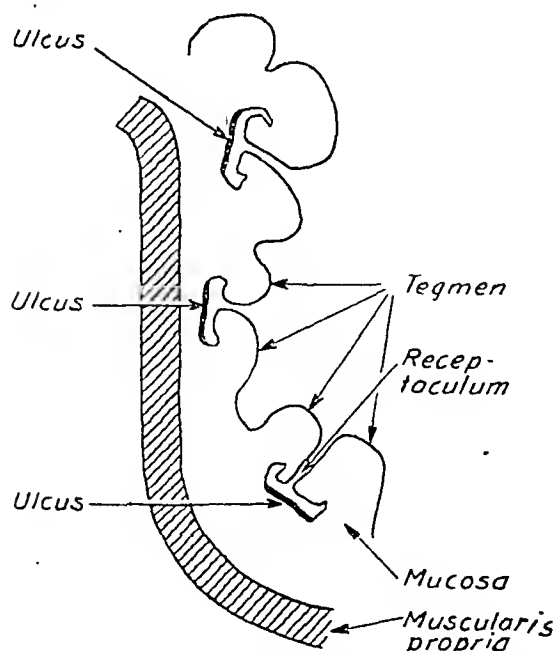


Fig. 1.—Schematic drawing of fold formations of the mucosa around tuberculous ulcerations in the intestines. (After Tisell.)

wise disappears rapidly. The schematic drawing (figure 1), reproduced here from Tisell, shows that tuberculous ulcers in the intestines

Present series of investigations

The material.—In the present series, 163 patients were examined all of whom had pulmonary tuberculosis but two, one having cervical adenitis and one, though admitted for abdominal tuberculosis, having sprue; these two cases are included in the tables where not otherwise stated.

All the patients were Indians except the following 12: one European, one Chinese, one Chino-Burman, and nine Anglo-Indians, of whom only one, an Anglo-Indian, was found x-ray positive for intestinal tuberculosis.

Method used.—Patients were given one of the standard preparations of opaque barium meal, six ounces of barium sulphate stirred up in one pint of water. During the beginning of the series an enema was given either the night before or in the early morning but it was later dispensed with. The first x-ray examination was done 4 hours after the ingestion of the barium meal, and then repeated as often as necessary within the next 3 or 4 hours; the patients were seen again at the 10th, 11th or 12th hour but after that only in special cases. The 24 hours' examination was omitted, as in all cases a filling defect or the absence of it could be demonstrated within the time stated, and the condition of the cæcum at

24 hours was considered of no certain additional value to the diagnosis.†

Findings on x-ray.—An x-ray negative diagnosis was made in 99 cases, 74 cases appearing normal and 25 doubtful; an x-ray positive diagnosis of intestinal tuberculosis was made in 64 cases, based upon following observations.

(a) *Filling defects.*—A typical filling defect was seen exclusively in the 64 cases, being extensive and involving the whole of the cæcum and the adjacent half or the whole of the ascending colon in 38, in six of which the spasm was so severe as to correspond to Stierlin's sign; in 12 the main feature was a definite reduction in size and volume of the cæcum and the ascending colon, but the outline was less ragged than in the former group, the wall appearing rather rigid; in 13 the changes were confined to a small area of the cæcum or the ascending colon; one case showed changes mainly in the descending colon. Fleischner's sign was found in seven cases.

(b) *Motility.*—In the first four tables the cases have been grouped according to the position of the barium column at certain hours.

TABLE I

Position of head of barium column at various periods of observation after ingestion of barium meal, related to x-ray finding of filling defects

Position of head of barium column	No filling defect found (99 cases)			Typical filling defect found (64 cases)		
	4 or 5 hours	6 or 7 hours	10, 11 or 12 hours	4 or 5 hours	6 or 7 hours	10, 11 or 12 hours
Ileum	9	1	0	8	1	1
Cæcum	10	2	0	4	1	0
Ascending colon	21	11	1	8	3	1
Transverse colon	34	33	13	15	13	1
Descending colon	14	23	32	20	24	17
Pelvic colon or rectum	5	11	47	5	11	38
Observations not recorded	(6)	(16)	(6)	(4)	(11)	(6)

TABLE II

Frequency of cases showing barium in the descending colon at various hours related to x-ray finding of filling defects

Hours after ingestion of barium meal	CASES WITHOUT FILLING DEFECT			CASES WITH FILLING DEFECT			P*
	Number examined	Cases with barium in descending colon		Number examined	Cases with barium in descending colon		
		Number	Percentage		Number	Percentage	
4 or 5 hours ..	93	19	20.4	60	25	41.7	0.008
6 or 7 hours ..	83	34	84.9	53	35	66.0	0.012
10, 11 or 12 hours ..	93	79	41.0	58	55	94.8	0.61

* The statistical value of the various observations is appended for tables where doubt may arise. The probability (P) of the observations being due to chance has been estimated by the Chi-square test; in instances of observations with figures less than five two adjacent columns have been amalgamated and in case of fourfold tables the exact treatment given in R. A. Fisher's 'Statistical Methods for Research Workers', 8th ed., 1941 has been used; for other fourfold tables Yates' correction has been used. The level of significance was considered at P=0.05, smaller values increasing the significance.

† Barium enema was used to begin with in addition to the barium meal but as it did not yield more information than already obtained by the meal, it was abandoned as a routine measure. In a number of cases where the diagnosis was uncertain, the examination was repeated.

In table I is shown in how many cases the meal head was observed at various sections of the digestive tract, table II giving the percentage of cases in which the meal head had passed into the descending colon at the 6 or 7 hours' examination. Tables III and IV indicate the position of the tail end of the barium column at the last period of examination. In each table the cases have been grouped according to the finding of filling defects.

It may be seen from table I that, in cases showing filling defect, the barium column had generally advanced to a point further down in colon than in cases without filling defect observed at the same hour. This is more clearly seen when choosing for comparison the frequency with which a certain point, *e.g.* the descending colon, is reached. This is shown in table II.

From table II it is evident that there is a significant difference in motility between cases without filling defect and those with filling defect within the first 7 hours. Similarly, if the cases are examined in relation to the evacuation of the cæcum at 10 to 12 hours as is done in table III, there will be seen to be a definite association between early evacuation and filling defect.

TABLE III

Evacuation of the cæcum related to x-ray finding filling defect

Cæcum at 10, 11, or 12 hours	Number examined	CASES WITH FILLING DEFECT		
		Number	Percentage	
Barium present	118	37	31.4	(P = 0.003)
Empty	45	27	60.0	

Whereas it has been shown in tables I to III that cases with filling defect often had a more rapid passage of the barium than cases without filling defect, it may be seen from table IV that a delayed passage can also be associated with filling defect.

TABLE IV

Retention of barium in the ileum related to x-ray finding of filling defect

Ileum at 10, 11, or 12 hours	Number examined	CASES WITH FILLING DEFECT		
		Number	Percentage	
Empty	137	50	36.5	(P = 0.02)
Barium present	18	13	76.2	

In view of the importance ascribed to hypermotility as stated above, a comparison is given

in table V between the observations of cases with barium in the descending colon at the 6 or 7 hours' examination in the present series and relevant observations by Brown and Sampson (1930). The figures for the latter have been compiled from Brown and Sampson's tables referring to their 180 post-mortem and operation checked cases.

TABLE V

Hypermotility as indicated by barium having reached the descending colon within 6 or 7 hours, related to filling defect

Brown and Sampson's series compared with the present one

	Number of cases examined	CASES WITH BARIUM IN DESCENDING COLON		
		Num- ber	Per- centage	
	(a) Cases without filling defect			
Brown and Sampson. Present series	89	7	7.9	(P<0.001)
	83	34	41.0	
(b) Cases with filling defect				
Brown and Sampson. Present series	87	48	55.2	(P>0.20)
	53	35	66.0	

It may be seen from table V that there is a striking difference between Brown and Sampson's series and the present series with regard to motility in patients showing no filling defect, the group of Indian patients showing nearly five times as many cases with barium in the descending colon as compared with the American group. In the group with filling defect there is no significant difference.

From their findings Brown and Sampson rightly conclude that hypermotility is a factor very closely related to filling defect and therefore of much importance in the diagnosis of intestinal tuberculosis. Though the present material also shows such an association, the closeness of the association is not nearly so marked. There are so many cases with a rapid passage of the barium showing no filling defect, and so many cases with filling defect but without a rapid passage of the barium, that in individual cases motility cannot be used either for a positive or a negative diagnosis of intestinal tuberculosis. Therefore, in this paper a positive x-ray diagnosis has been based upon the finding of a typical filling defect only.

In adopting this standard for a positive diagnosis, it is of course recognized that it is possible that some x-ray positive cases may not really be intestinal tuberculosis, and in some x-ray negative cases the complication may be

present. Whether this was so could be determined only by autopsy control.

The possibility that the increased motility in the x-ray negative group of the present series as compared with that of the American might be due to non-tuberculous intestinal diseases has been investigated with regard to ankylostomiasis and chronic amoebic dysentery. In 50 of the 163 patients, hookworm ova were found, but they showed no significant association with either filling defect or hypermotility.

Though some of our patients gave a history of chronic dysentery, in no instance was *Entamoeba histolytica* or cysts found in the x-ray positive cases, and in only two of the x-ray negative in which amoebae were found 2 and 9 months prior to the x-ray examination respectively. Ukil (1942) found in a material of 50 cases of pulmonary tuberculosis examined by barium meal, ten cases with chronic amoebic dysentery, cysts being demonstrated. X-ray examination revealed caecal spasm in five but nothing abnormal in the other five cases; none of these cases were x-ray positive for intestinal tuberculosis. In neither of the two series of Indian patients has therefore any relation been found between typical filling defect and chronic amoebic dysentery, nor can hypermotility in the present series be explained by amoebic dysentery.

If not due to any pathological condition of the intestines it is possible that the rapid passage of the barium is a normal physiological phenomenon in Indian patients, or it may be caused by certain constituents in their diet. P. V. Benjamin making similar observations by the x-ray method on patients in this sanatorium before the present series was begun, has suggested (personal communication) that the hypermotility may be caused by the high content of chillies and spices in the Indian diet. In the absence of a control material of normal Indians it is, however, not possible to verify this theory.

Incidence of intestinal tuberculosis

The first group of the present series included mostly selected cases in whom intestinal tuberculosis was suspected, about half showing on x-ray examination definite signs of intestinal tuberculosis, as may be seen from table VI. Since this appeared to be a high proportion of positive cases, a special investigation was carried out to determine the true incidence of the disease among the patients. The second group of the present series includes therefore about a hundred patients selected at random, only two or three very ill patients being omitted. The results are given in table VI.

Ten patients appear in the unselected as well as in the selected group. The reason is as follows. In order to ensure that the latter group should be fully representative of all the patients in the sanatorium, lots were drawn, and in ten cases the lot fell on patients of the selected group already examined. It is clear that to omit from the unselected group these ten suspicious cases would bias the sampling.

From table VI it may be seen that the incidence of intestinal tuberculosis among a group of patients of the type commonly met with in this sanatorium was 31.1 per cent, whereas among a group of patients specially selected it was as high as 52.8 per cent. It is not permissible to conclude from these figures and similar ones from other sanatoria what is the difference in incidence between a group of predominantly Indian patients and European patients, since the type of patients in an institution depends entirely upon the policy governing the admission of patients.

For the purpose of further analysis the two groups have been pooled in order to allow a division of the material into more sub-groups. The total group of 163 patients therefore represents a certain selection, more x-ray positive cases being included than normally found; at

TABLE VI
Incidence of intestinal tuberculosis among patients in the Union Mission Tuberculosis Sanatorium

Group of patients	X-RAY EXAMINATION FOR INTESTINAL TUBERCULOSIS				
	Negative cases		Positive cases		Total
	Normal	Doubtful	Mild	Advanced	
Selected Total	22 33, or	11 47.2%	4 37, or	33 52.8%	70
Unselected Total	55 71, or	16 68.9%	9 32, or	23 31.1%	103
Cases common to sselected and unselected groups	3	2	0	5	10
GRAND TOTAL	74	25	13	51	163

each step of the following analysis the total material was compared with the group of unselected patients, and it was found that the former led to the same conclusions as the latter, the only difference being that the significance increased with the larger material.

Ætiology of secondary intestinal tuberculosis

In order to determine the importance of some factors which may influence the development of intestinal complications in patients with pulmonary tuberculosis, the present material has been analysed with regard to age, sex, degree of pulmonary involvement, presence of cavities, number of bacilli in the sputum and duration of pulmonary illness, as shown in tables VII to XI.

TABLE VII

Age in years		X-RAY OF INTESTINES.			
		Number examined	Positive cases		
			Number	Per-centage	
(a) Age					
10-	..	23	7	30.4	(P > 0.70)
20-	..	86	34	39.5	
30-	..	37	15	40.5	
40-50	..	17	8	47.1	
(b) Sex					
Male	..	119	47	39.5	(P > 0.80)
Female	..	44	17	38.6	

From table VII it may be seen that no association was found between age and sex on the one side and intestinal tuberculosis on the other. Comparisons between age and sex revealed nothing further.

Judging from previous investigations it was expected to find a clear connection between the extent of the pulmonary process and the incidence of intestinal tuberculosis. This was however not the case as table VIII shows. Though there appears to be a tendency towards the more advanced forms having a higher incidence, the differences are far from being significant.

The two x-ray positive cases in table VIII without any active lesions in the lungs were predominantly abdominal cases, and might perhaps be considered cases of primary intestinal tuberculosis rather than of the secondary type. Their exclusion from the material would, however, not alter the conclusion that in cases with active pulmonary tuberculosis, the amount of lung tissue affected as judged by x-ray examination had no definite association with the incidence of intestinal tuberculosis. The same negative conclusion is arrived at from studying the relationship of cavities in the lungs to the incidence of intestinal

TABLE VIII

Incidence of intestinal tuberculosis related to the degree of pulmonary involvement

Lungs	X-RAY OF INTESTINES			
	Number examined	Positive cases		
		Num-ber	Per-centage	
No pulmonary tuberculosis, or a few inactive foci only.	11	2	18.2	(P > . 0.30)
Localized active process within one lobe.	38	13	34.2	
Greater part of one lobe, possibly with moderate spread to other parts.	42	18	42.9	
Two lobes or more.	72	31	43.1	

tuberculosis as shown in table IX. By cavities is meant whether cavities were found at any time even though at the time of barium examination the cavity might appear closed.

TABLE IX

Cavities in the lungs in relation to intestinal tuberculosis

Cavity	X-RAY OF INTESTINES			
	Number of cases*	Positive cases		
		Number	Per-centage	
Found ..	136	57	41.9	(P = 0.29)
Not found	25	7	28.0	

* Excluded two non-pulmonary cases.

Though suggestive of an association between cavities and intestinal tuberculosis, the difference between the groups is not definitely significant. Another reason for the relative high number of positive cases in the non-cavity group may possibly be that in some cases undetected cavities were present. Gardner in his post-mortem material found a significantly higher proportion of intestinal tuberculosis among cavity cases than in those without cavities; 148 positive cases among 173 of the first group against 11 out of 21 in the latter. In view of this observation it would be interesting to collect a larger material of obvious non-cavity cases.

The reason why we should expect a much closer association between cavities and intestinal tuberculosis is that lesions with cavities produce more

secretion and a greater output of tubercle bacilli than mere infiltrative or fibrosed lesions without cavities. It is generally agreed that tuberculous inflammation and ulceration of the intestines, particularly of the ileo-cæcal region, is caused by a prolonged and intimate contact of the mucous membrane with bowel contents mixed with virulent bacilli. A suggestion that this may be true is given by the findings of table X.

TABLE X

Tubercle bacilli in the sputum related to intestinal tuberculosis

Tubercle bacilli	X-RAY OF INTESTINES			
	Number examined	Positive cases		
		Num- ber	Per- cent- age	
Not found ..	13	2	15.4	(P = 0.06)
Found by culture of sputum or stomach-wash water, or by a single smear only.	19	6	31.6	
Occasionally found, or absent for several months.	53	22	41.5	
Present con- tinuously.	78	34	43.6	

That the differences in table X are smaller than expected may be explained by the findings of tubercle bacilli in the sputum being only a poor indicator of the number of bacilli which enter the digestive tract.

TABLE XI

Duration of illness (pulmonary tuberculosis)

Duration of pulmonary symptoms (years)	X-RAY OF INTESTINES			(P = 0.11)
	Number examined*	Positive cases		
		Number	Percentage	
0-	23	8	34.8	
$\frac{1}{2}$ -	43	12	27.9	
1-	47	23	48.9	
2-	28	15	53.6	
4-8	20	6	30.0	

* Omitted two cases : one with cervical adenitis, the other with sprue.

Although the differences are too small to justify definite conclusions, it appears from table XI that it is mostly cases of one to three years' duration which present intestinal complications.

It is reasonable to think that it would take some time for these to develop, but it is surprising to find that more than 30 per cent of cases with symptoms of less than 6 months' duration were affected. It may, however, be said that an estimate of the duration is generally less accurate in the beginning of the illness, patients often understating the length of time they have had their symptoms, than in cases of longer duration where the patients have been under treatment or observation for a known period of years either by their own doctor or in an institution. It is not so unexpected that patients who have been sick for 4 years or more appeared to be less frequently affected than those of shorter duration, because they represent cases of a fairly high resistance as evidenced by their surviving the dangerous first 2 or 3 years of illness when the mortality rate is highest.

Summing up, it may be said that although the degree of pulmonary involvement, the duration of the disease and the number of bacilli excreted from the lungs seem to have a bearing upon the development of the intestinal complications, the present material shows a greater uniformity than was anticipated in view of other investigations. This may be due to something characteristic for the type of tuberculosis generally met with in Indian patients, at least as we see them in this sanatorium where fewer cases either of the early type or of the late fibrotic type are represented than in many sanatoria in Europe and U.S.A., the majority of the cases being a predominantly exudative type.

Significance of clinical symptoms

Taking the clinical features commonly met with in intestinal tuberculosis and analysing their importance for the diagnosis using the x-ray findings as criterion, we see first from table XII that loss of weight is closely associated with the presence of intestinal tuberculosis.

TABLE XII

Weight

Weight	X-RAY OF INTESTINES			
	Number examined	Positive cases		
		Num- ber	Per- cent- age	
Normal ..	42	5	11.9	(P < 0.001)
Subnormal :—				
(a) Gaining ..	86	36	41.9	
(b) Losing or stationary.	35	23	65.7	

From table XII it may also be seen that not only is there a significant difference between cases of normal weight including patients with overweight, and those showing loss of weight, but

within the subnormal group itself a significant difference is found between those with an increasing weight curve against those with a stationary or declining curve. It is quite remarkable that in this latter group as many as two out of three patients had intestinal tuberculosis.

Studying next fever as a symptom of intestinal tuberculosis, it may be seen from table XIII that also here is a clear association found between the symptom and the disease. Sporadic attacks of fever lasting only a few days have been disregarded; by low fever is understood a morning temperature about 98 to 99°F. and an evening temperature about 101 to 101.5°F., moderate temperature again 99 to 99.5/102 to 102.5, and by high fever temperatures above this range. The temperature curve for the last one to two months prior to the barium meals was taken into consideration.

TABLE XIII
Fever

Temperature		X-RAY OF INTESTINES			
		Number examined	Positive cases		
			Number	Percentage	
Normal ..	78	15	19.2	(P < 0.001)	
Low fever ..	49	23	46.9		
Moderate fever	27	21	72.2		
High or intermittent fever.	9	5			

It should be noted that, despite normal temperature, nearly 20 per cent of the patients had intestinal complications; it is evident that the incidence increases with the degree of fever.

In table XIV are entered cases with diarrhoea; only periods of one month or more have been considered, a single attack or two of diarrhoea being ignored.

TABLE XIV
Diarrhoea

Diarrhoea		X-RAY OF INTESTINES			
		Number examined	Positive cases		
			Number	Percentage	
Nil	..	92	23	25.0	(P < 0.001)
Occasionally	..	39	18	46.2	
Often	..	20	13	65.0	
Daily	..	12	10	83.3	

There is obviously a close association between diarrhoea and intestinal tuberculosis though the

symptom cannot be regarded as specific for tuberculosis. Of the two cases with daily and persistent diarrhoea, the one had chronic sprue of eight years' duration; the other had a rapidly progressing tuberculosis with marked toxæmia leading to death only 13 days after the barium examination.

It may also be seen from table XIV that the absence of diarrhoea does not exclude intestinal tuberculosis which was found in 25 per cent of cases with no diarrhoea. Some of the patients suffered from constipation which could be directly ascribed to a chronic intestinal tuberculosis; one case had his pulmonary tuberculosis discovered only after having been treated by his doctor for a long time for chronic constipation (see figure 7, plate XXVI). Cases with diarrhoea alternating with constipation were not commonly seen.

In table XV are included under the term 'dyspepsia' such symptoms as loss of appetite, vomiting, cardialgia, belching, and simple dyspepsia. This group of symptoms shows also a definite association with the presence of tuberculosis of the intestines; but again, it is remarkable to find nearly one-third of the positive cases without any dyspeptic symptoms.

TABLE XV
Dyspepsia

Dyspepsia		X-RAY OF INTESTINES			(P < 0.001)
		Number examined	Positive cases		
			Num- ber	Per- cent- age	
Absent	..	88	21	23.8	
Present	..	75	43	57.3	

It may also be seen that it is only a little more than half of the cases with dyspeptic symptoms who have intestinal tuberculosis; in the remaining 42.7 per cent the intestines appeared normal.

Taking finally the general clinical impression of the patient's condition it may be seen from table XVI that when the condition remains

TABLE XVI
General condition

General condition	X-RAY OF INTESTINES			(P<0.001)
	Number examined	Positive cases		
		Number	Percentage	
Good ..	83	17	20.5	
Fair ..	56	30	53.6	
Poor ..	24	17	70.8	

1930, as evidenced by a brief notice by C. Frimodt-Møller (1930), patients in this sanatorium with intestinal tuberculosis have received treatment with vitamin-rich food and heliotherapy besides ordinary symptomatic treatment. A number of cases have had pneumo-peritoneum.

Though it would be difficult to subscribe a specific effect to the treatment with vitamin-rich food and heliotherapy on the course of intestinal tuberculosis, we have had no reason to withdraw the treatment from such cases, as it may probably have a beneficial general effect. The present material does not allow any conclusions regarding the effect of such treatment; that would require a special investigation extending over some years.

Conclusion

In conclusion the following points may be mentioned about the method of x-ray diagnosis of intestinal tuberculosis which are as true for Indian patients as for those in the West. Firstly, it is a comparatively easy, cheap and simple, though time-consuming, method; secondly, it is remarkably consistent as judged by repeated examinations of the same individuals; thirdly, it conforms surprisingly well with the clinical picture; fourthly, it yields information of much value in cases where other methods fail.

The crucial question is, of course, how correct is the diagnosis arrived at by the x-ray method. A study of reports on comparative investigations between x-ray and post-mortem findings shows a strikingly high agreement in patients with pulmonary tuberculosis, but the method, like all other x-ray examinations of pathological conditions, has its limitations, and the diagnosis can never be made with absolute accuracy. Still, it is reasonable to ascribe a high degree of certainty to a positive diagnosis whereas it may have a slight limitation in negative cases. The number of cases with intestinal involvement missed by the x-ray method cannot be many, and probably are so few as to be of academic rather than practical interest.

The method is essential for any rational work on intestinal tuberculosis, and it should be used to a much greater extent than has hitherto been done in many places.

Summary

(1) Of a group of 163 patients, mostly Indians, all of whom but two had pulmonary tuberculosis, 64 showed definite radiological signs of secondary intestinal tuberculosis.

(2) The x-ray diagnosis was based upon demonstration of typical filling defects in the ileum, caecum and ascending colon especially.

(3) Rapid passage of the barium through the colon was found associated with the finding of filling defect, although hypermotility was found in x-ray negative cases more frequently than is reported for European patients.

(4) Of 103 unselected cases, 32, or 31.1 per cent, had intestinal tuberculosis.

(5) The frequency of intestinal tuberculosis increased with the severity of the pulmonary disease, so much so that far advanced cases can be said to be affected in a very high percentage; on the other hand, even in apparently healthy patients the possibility of intestinal involvement cannot be ruled out.

(6) A good agreement was found between the radiological diagnosis and clinical symptoms characteristic of intestinal tuberculosis.

(7) The prognosis, though certainly more unfavourable for cases with intestinal tuberculosis, should not be regarded too pessimistic, as many cases undoubtedly fare well despite their abdominal complication.

Illustrative cases

Case 1.—Z. J., male, 24 years. Admitted 27th October, 1942, bilateral pulmonary tuberculosis, diagnosed one year earlier. Had on right side a contralateral pneumothorax with the upper lobe adherent to the dome of the pleura; pleural effusion was repeatedly aspirated in order to get the lung re-expanded. Upper third of left lung was affected and a cavity was found in the infraclavicular region. The temperature showed an irregular course with frequent periods of moderately high fever. No abdominal complaints.

Routine x-ray examination with barium meal on 25th February, 1943.—4½ hours: meal-head at right colic flexure; the caecum and ascending colon showed marked defective filling. 5½ hours: barium in transverse colon; x-ray photo taken (figure 2, plate XXV). 8 hours: meal-head in iliac colon; the caecum and most of ascending colon appear typically 'sponge-like'. 11 hours: the ileum is empty; meal-head in ampulla recti; caecum and ascending colon show still typical defective filling. Diagnosis: ileo-caecal tuberculosis.

Next day, on 26th February, 1943, inducement of an artificial pneumothorax on the left side was attempted but the pleural space was found obliterated; about five minutes later the patient had slight twitching of the hands and died in a minute or two with signs of an air embolus.

Autopsy, 3 hours after death, after intra-arterial injection of formalin. Thorax: heart and pericardium apparently normal; right lung and pleura: a large pneumothorax cavity with thickened, almost leathery pleura covered by fibrous deposits; the posterior and apical surface of the lung firmly adherent to the chest-wall; right upper lobe atelectatic and fibrosed with a large irregular cavity in its apex; the two other lobes contained numerous productive tubercles from miliary to hemp-seed size. Left lung and pleura: pleura adherent all over; at the site of the pneumothorax puncture in the left axilla, a fresh clot of blood was found lying in close vicinity to the lower edge of a rib. Left lung showed extensive tuberculosis in the upper lobe with a moderately fresh cavity, about 3 inch in diameter; scattered spread in lower lobe.

Abdomen: peritoneum normal. Distal part of ileum and colon as far as the proximal part of the transverse colon was removed *in toto* and placed in formalin. After rinsing, the specimen was filled with barium emulsion and x-ray photographed (figure 3, plate XXV); afterwards it was cut open, washed and photographed (figure 4, plate XXVI).

Ileum appeared normal. The colic valve was thickened. The caecum and ascending colon were very hyperplastic with extensive fold formation and numerous small elevated areas; between the folds deep clefts and grooves. Only beyond the right colic flexure did the colon assume a normal appearance. Appendix: two to three typical tuberculous ulcerations.

Case 2.—G., female, 21 years, pulmonary tuberculosis. Barium examination: (5½ hours) (figure 5, plate XXVI).

(Concluded on opposite page)

PLEURAL EFFUSION IN PNEUMOTHORAX TREATMENT

(STATISTICAL SURVEY)

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PLEURAL effusion is the commonest complication of pneumothorax treatment. Artificial pneumothorax now occupies the foremost place in the treatment of lung tuberculosis, and its value is so much appreciated by the patients themselves that, when a case is considered unsuitable for this treatment, the patient always despairs about his ultimate recovery. But with all its popularity, the collection of 'fluid' is still a bugbear to many patients. This fear is not absolutely without foundation, because in some cases the fluid does become purulent and causes

(Continued from previous page)

typical filling defect confined to the cæcum and the adjacent half of ascending colon, which appear narrow, constricted with a very ragged and nibbled outline. Distal half of the ascending colon shows normal haustration.

Case 3.—D., male, 28 years : pulmonary tuberculosis : frequent attacks of diarrhoea for one year. Barium meal examination : (4½ hours) (figure 6, plate XXVI); the cæcum and ascending colon show a typical filling defect; the outline of the colic valve is clearly seen as a large semi-circle (Fleischner's sign); terminal ileum very spastic and string-like.

Case 4.—K. K., male, 41 years, had dyspepsia and constipation two years prior to the diagnosis of pulmonary tuberculosis. Barium meal examination (7 h.p.c.) (figure 7, plate XXVI); the cæcum and ascending colon extremely spastic and irregular; obstructed passage of the barium through the colic valve was evident.

Figure 8 (plate XXVI). Normal case.

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prolonged misery and suffering. A study of effusion in all its aspects is therefore essential with a view to preventing or limiting its formation. The subject covers a wide field and we shall confine ourselves to certain aspects of the problem as observed in 250 artificial pneumothorax cases at Jadabpur Tuberculosis Hospital from 1938 to 1941.

Ætiological factors.—Clinical and cytological tests indicate that pleural effusion is more of the nature of an inflammatory exudate than simple transudate. The exudate, when it first forms, is usually sterile on ordinary culture media, but by the employment of special cultural methods as well as by animal inoculation, the tubercle bacillus has almost invariably been detected. Of the many factors which have been put forward as being responsible for fluid formation, the most important is the separation of pleural layers by gas, with consequent stretching and perhaps rupture of adhesions. The adherent pleura usually provides the surface tubercles with a protective barrier, and as a result of separation of the layers, these tubercles burst into and infect the pleural cavity. We shall refer to this subject while dealing with adhesions. Other contributory factors which have been mentioned are : the irritation caused by local anæsthetic, the nature and the temperature of the gas introduced, the injury caused by repeated punctures, and lastly, infection from outside. We shall discuss some of these factors as we present our statistics.

As a rule, a local anæsthetic was not used in our series after the first 3 or 4 fillings except where the patient was extremely nervous. The coldness of the air introduced has been mentioned as a cause of effusion. In order to counteract this, we used to warm the air by passing the tube through a thermosflask containing hot water. As the effect on effusion was not appreciable, this practice has been given up.

Incidence of effusion.—The figures published by different authorities on this subject vary widely. To quote only a few; in Burrell's (1932) series it is 41.4 per cent; Riviere (1927) about 50 per cent; Saugman (1914) 67.2 per cent and Dumarest and Brette (1929) 70.3 per cent. The cause of this divergence appears to lie in the method of observation employed. Those who made routine radiological examinations of all cases before and for some days after each refill have recorded the highest percentage; even the smallest amount of fluid, an amount that just fills the costo-phrenic angle for a transitory period, has not escaped them. On the other hand, those who have made only a casual examination, or only when signs and symptoms were suggestive, have naturally recorded less.

In our series, the routine was to screen all artificial pneumothorax cases after the 4th filling, and thereafter once a month unless for special reasons more frequent examinations were necessary. The figures for our 250 cases are

given in table I. We have classified the effusion into 'large' and 'small' according to whether it covered the dome of the diaphragm or not.

TABLE I
Incidence of effusion in 250 cases

Extent of effusion	Number of cases	Percentage
(i) Large effusion, i.e. large enough to cover the dome of the diaphragm in the erect position.	85	34.0
(ii) Small effusion, i.e. effusions below this level including transitory effusions.	66	26.4
(iii) All effusions (small and large).	151	60.4

In 4 cases the effusion developed in the contralateral side of the chest and not in the pneumothorax side. In addition to the usual symptoms of fluid formation, the special feature in all these cases was a varying degree of dyspnoea.

We shall now proceed to consider the incidence of effusion in relation to the extent, situation and character of the disease. Table II shows the position at a glance.

TABLE II
Effusion in relation to extent, situation and character of the disease

Subject	Number of cases	Large effusion	Small effusion	Total
(i) Extent of disease— Turban-Gerhardt : Stage 2	31 12.4%	11 38.7%
Stage 3	219 87.6%	140 63.9%
(ii) Site of disease— Central	28 11.2%	6 21.4%	7 32.1%	15 53.5%
Peripheral	222 88.8%	79 38.1%	8 23.1%	135 61.2%
(iii) Character of the disease— Exudative	242 96.8%	146 58.4%
Productive	8 3.2%	5 41.6%

From a study of table II we find that the smaller the area of the lung involved, the lower is the incidence of effusion (38.7 per cent in stage 2 as against 63.9 per cent in stage 3).

The lesions situated nearer the pleural surface are more likely to cause effusion than those situated more centrally (61.2 per cent : 53.5

per cent). Moreover, central disease produced smaller effusions. The incidence of large effusions was 21.4 per cent in central and 38.1 per cent in peripheral disease.

The exudative type of disease is more likely to produce effusion than the productive type (58.4 per cent : 41.6 per cent). The number of productive cases in our series was, however, too small for comparison.

Adhesions and effusions.—The subject is important because stretching and rupture of adhesions are believed to play a prominent part in the production of large effusions. This idea is based on the fact that when an adhesion bursts spontaneously or is cauterized by galvano-cautery, effusion always forms. In the process of stretching, some injury is bound to occur at the parietal or pulmonary attachments. This, together with the bursting of a tuberculous focus or the tearing of lung tissue, will easily evoke an exudative response in the pleura of an allergic subject.

In order to study the incidence of effusion in relation to the amount of stretching, we have classified the adhesions in table III according to their shape and size as seen on postero-anterior skiagrams of the chest. It is needless to say that the appearance of adhesions seen in one plane is extremely deceptive, and often does not correspond to their actual appearance as visualized through a thoracoscope.

From a study of table III it would appear that even where no adhesions were present, effusion developed in 56.2 per cent. In approximately half of these cases, the effusion was fairly large.

Where adhesions were present, the percentage of effusion was higher (*vide* group 5 in the

table). There was 8.7 per cent increase in large effusions and 6 per cent in the total.

Short thick bands occurred in about 50 per cent of our cases, and this group recorded the highest percentage (66.3) of effusion. Long string-like bands, on the other hand, were responsible for the maximum number of large effusions (46.1 per cent).

We may conclude that even in the absence of adhesions, the probability of fluid formation exists in more than half the cases although the risk is somewhat greater when adhesions are present.

The fact that stands out prominently in this table is that by far the largest number of effusions (71.4 per cent), whether small or large, developed within 3 months of the beginning of treatment. The percentage of new effusions decreased with the length of treatment, and about 80 per cent of effusions developing after 3 months were large effusions. Small and transitory effusions were a feature of the early months and never occurred after 6 months in our series.

Fever and effusion.—The onset of effusion was usually accompanied by headache, malaise, vague

TABLE III
Adhesions and effusions (236 cases)

Type of adhesion	Number of cases	Large effusion	Small effusion	Total
(1) No adhesion	48 20.3%	14 29.1%	13 27.1%	27 56.2%
(2) String-like adhesions at least 2 inches long	26 11.2%	12 46.1%	2 7.7%	14 53.8%
(3) Short and thick bands of various shapes and sizes.	116 49.1%	43 37.0%	34 29.3%	77 66.3%
(4) Pleural surfaces entirely adherent for some distance including cases of contra-selective collapse.	46 19.4%	16 34.7%	10 21.8%	26 56.5%
(5) Adhesions of all types	188 79.7%	71 37.8%	46 24.4%	117 62.2%

Intra-pleural pressure.—As a rule, we found negative pressure quite sufficient to maintain the desired collapse in a large majority of cases. The highest percentage of effusion also occurred with negative pressure (*vide* table IV).

TABLE IV
Intra-pleural pressure and effusion (237 cases)

Mean intra-pleural pressure	Number of cases	Percentage of cases	Incidence of effusion
Negative ..	178	75.1	111 (62.3%)
Zero ..	9	3.8	4 (44.4%)
Positive ..	50	21.1	23 (46.0%)

This shows that positive pressure, by itself, does not play any part in the formation of fluid.

Time interval and effusion.—Table V shows the time interval between the induction of artificial pneumothorax and the onset of effusion. The average number of air injections before the onset of effusion was 11.5, the smallest being 1 and the largest 49.

pains and some degree of pyrexia. The rise in temperature (oral) is considered in table VI.

TABLE V
Time interval and effusion (126 cases)

Time interval since induction of AP	Number of cases	Large effusion	Small effusion	All effusions
Within 3 months	90	46 36.5%	44 34.9%	90 71.4%
3 to 6 months ..	25	18 14.3%	7 5.5%	25 19.8%
6 months to 1 year	9	9 7.1%	Nil	9 7.1%
Over 1 year ..	2	2 1.5%	Nil	2 1.5%

34.8 per cent of effusion were 'cold', *i.e.* not associated with any rise of temperature. The remaining 65.2 per cent were 'hot', *i.e.* accompanied by varying degree of fever. The bulk of the hot effusions (70.7 per cent) were large.

The average time taken by the fever to come down to the previous level was 17 days—the longest being 9 weeks and the shortest 2 days.

TABLE VI
Fever and effusion (132 cases)

Degree of fever	Number of cases	Large effusion	Small effusion	All effusions
No rise of temperature.	46	19 14.4%	27 20.4%	46 34.8%
Rise not exceeding 2°F.	38	23 17.4%	15 11.4%	38 28.8%
Rise exceeding 2°F.	48	38 28.8%	10 17.6%	48 36.4%

Fate of effusion.—Unfortunately our records in regard to character, cytological and bacteriological tests of effusion are incomplete, and we do not propose to discuss these questions. We shall consider in this section the problem of absorption of effusion with or without interference and the time factor in absorption.

TABLE VII
Absorption of effusion (131 cases)

Subject	Number of cases	Large effusion	Small effusion	Total
Effusion absorbed without affecting the course of AP treatment.	49	16 12.2%	33 25.2%	49 37.4%
Absorption followed by obliterative pleuritis. AP had to be abandoned.	33	25 19.1%	8 6.1%	33 25.2%
Patient left with residual fluid.	49	41 31.3%	8 6.1%	49 37.4%

62.6 per cent of effusions (82 out of 131 cases) were absorbed during the period of observation which ranged from 3 months to several years. In 25.2 per cent of effusion cases, obliterative pleuritis set in rendering further artificial pneumothorax treatment impossible.

Small effusions were not interfered with. 83.6 per cent of them (41 out of 49 cases) were absorbed spontaneously.

Of the large effusions, 50 per cent (41 out of 82) were absorbed. Aspiration was necessary in 55 per cent of these cases.

Interference in some shape or form such as aspiration, gas replacement, pleural lavage and oleo- or gelatino-thorax was required in 54.2 per cent of all effusion cases.

Time factor in absorption.—(a) Small effusions: average time taken for their absorption was 11.1 weeks, ranging from 1.5 to 32 weeks.

(b) Large effusions: spontaneous absorption occurred in 55 per cent, and the average period for this group was 17 weeks (minimum—7 weeks; maximum—54 weeks).

Absorption was helped by interference in the remaining 45 per cent. For this group, the average time was 23.6 (minimum—6 weeks; maximum—52 weeks).

Summary.—In this brief résumé we have presented a summary of our experience with effusion in pneumothorax based on a study of serial skiagrams and screen examinations. In relation to the importance of the subject the number of cases (250) is rather small. We have dealt broadly with effusion as such, leaving aside clinical and bacteriological aspects as outside the scope of this paper. In the absence of a fuller knowledge of the technique and the data of other sanatoria, and of a more exhaustive study of the subject, it will not be profitable to attempt a comparative study and discussion. We shall rest content by giving here a summary of our findings.

(i) Effusion occurred in 60.4 per cent of the pneumothorax cases: in 34 per cent it was large enough to cover the dome of the diaphragm.

(ii) The smaller the area of the lung involved the lower the incidence of effusion.

(iii) In 56.2 per cent of cases, the effusion developed in the absence of adhesions. Where adhesions were present the risk of fluid formation was probably somewhat greater.

(iv) 62.3 per cent of effusions developed with negative intra-pleural pressure.

(v) 71.4 per cent of all effusions formed within first 3 months of treatment.

(vi) 34.8 per cent of effusions were 'cold'. The rest were 'hot'.

(vii) 37.4 per cent of effusions were absorbed without affecting the course of artificial pneumothorax treatment. In 25.2 per cent, absorption was followed by obliteration of the pleural space, and artificial pneumothorax treatment had to be abandoned.

(viii) Spontaneous absorption occurred in 83.6 per cent of small and 45 per cent of large effusions. Interference in some form was needed in 54.2 per cent of all cases.

(ix) The average period required for the absorption of effusion was 11 weeks for small effusions and about 20 weeks for large effusions.

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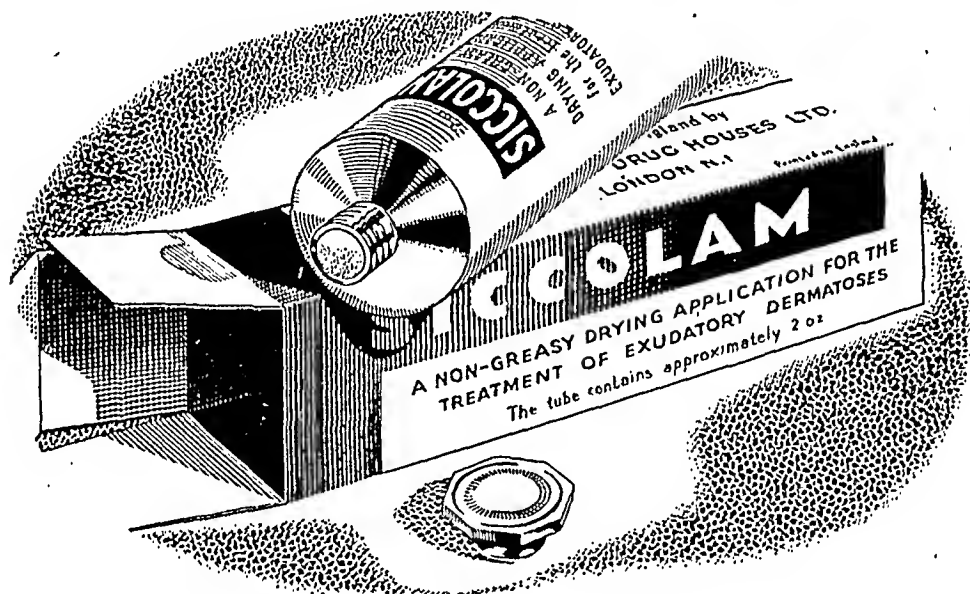
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Indian Medical Gazette

OCTOBER

ANTI-TUBERCULOSIS WORK

This is the sixth tuberculosis number of this journal, and it presents a suitable opportunity for a discussion of the present trends of thought on anti-tuberculosis work in general and of work in India in particular. We therefore think that the article by Dr. P. V. Benjamin published in our present number is a timely one.

Dr. Benjamin asks how much of the widely scattered anti-tuberculosis activity in India is being conducted as part of a well-thought-out plan, and how much will it contribute to the ultimate control and decline of tuberculosis. He states that there are places where the starting of isolated bits of tuberculosis work such as a clinic was considered all that was necessary, and he pleads that anti-tuberculosis work shall be carefully planned and developed in stages over a period of years with definite objectives in view.

Dr. Benjamin thinks that surveys of the incidence of tuberculosis are now less needed, and that the object of surveys should now be the detection of open and active cases which are the sources of new infection. He points out however that such work is very difficult and of very little use unless some provision is made for dealing with cases discovered, by treatment or isolation, or both. Such provision is now completely inadequate.

Dr. Benjamin discusses the tuberculosis clinic and states that no clinic is exercising its primary function unless it includes within its work a preventive programme. He thinks moreover that the diagnostic service should be separated from the treatment service. At present most clinics have a staff too small to deal adequately even with the work of diagnosis and treatment, and the preventive work outside the clinic is largely if not entirely neglected.

In other countries, the tuberculosis clinic has been one of a number of agencies working in co-operation, and without the other agencies the value of a clinic is greatly reduced. In India there has in some areas been seen the tendency to regard the clinic as being the most important if not the only agency needed. Dr. Benjamin also points out that of 819 cases diagnosed during the year at the New Delhi Clinic, 741 needed institutional treatment and that this was available for very few of them. Attempts to organize home treatment and isolation have not been very encouraging.

In other countries where the tuberculosis problem is now less serious than that of India, one institutional bed for 1,000 population is recommended. In India we have only a minute fraction of this number.

Dr. Benjamin's paper ends as follows: 'Much of the tuberculosis work in India hitherto has been a mere tinkering with the problem and with little real effect as regards control of the disease. With a tuberculosis problem so vast as that in India, it is impossible to begin with a full scheme all at once to be introduced in three or four years, and beginnings will have to be small, but these small beginnings must be part of a thought-out scheme for each area, to be introduced and developed as rapidly as possible, until every tuberculous patient is able to get the treatment he needs, not just for his own sake, but for the sake of preventing his being a source of infection to others. When we shall have reached this stage, and then only, we shall have made real headway in controlling tuberculosis in India'. We believe that Dr. Benjamin's views are those of most workers who have given the tuberculosis problem of India serious thought.

But even when we have adequate facilities for diagnosis and treatment and isolation of cases of tuberculosis, there will still be many problems to be solved. In England and Wales tuberculosis services are on the whole fairly adequate, but early diagnosis remains a problem. We quote here parts of review recently published on the report of the committee on tuberculosis in wartime appointed by the Medical Research Council of England at the request of the Ministry of Health. This review brings out numerous points of interest and importance which must be borne in mind in the carrying out of tuberculosis work in India in the future.

Five years ago, in an article in the *Practitioner*, Dr. Morland pointed out that two-thirds of the cases notified as suffering from pulmonary tuberculosis already had the disease in a moderately or far advanced form at the time of diagnosis. 'A few years ago I found, on investigating one hundred histories of consecutive cases drawn from the upper classes of society, that in only 40 per cent was the diagnosis made within three months of the first overt symptoms of the disease, and ten of these forty made the diagnosis easy by spitting blood'. Dr. Morland goes on to say that whilst the stethoscope rightly occupies a place of honour in clinical medicine, its uses do not include the elimination of pulmonary tuberculosis. 'If applied to this purpose it becomes a public danger, as most cases are no longer early by the time physical signs appear'. The important point is that early pulmonary tuberculosis has no physical signs and often no symptoms. Quite logically, D'Arcy Hart, in his Milroy Lecture in 1937, maintained that 'the mass examination by x-rays of groups of apparently healthy people was the only way of effectively increasing the proportion of cases diagnosed in the early stages of the disease'. In a leading article last January, the *Lancet* reminded us that people have been taught that tuberculosis is preventable, that early detection is simple, that treatment instituted in good time leads to arrest and recovery, that sanatorium treatment is available for all who may be unfortunate enough to become affected, and that a stay of a few months in delightful country surroundings will ensure an early return to home and duty. There is scarcely one of these teachings true in a strict sense; for it is impossible to prevent infection in the community as a whole; the early detection of the disease is one of the most formidable problems confronting doctors, and treatment cannot be instituted in good time for the

great majority of cases, because the lesions are relatively advanced when they are first detected. In a further leader in the *Lancet* of March 21, 1942, it is pointed out that, if the whole method of radiography is not to be discredited, 'and if hardships and misery from faulty diagnosis are to be eliminated, as much thought must be given to the training of personnel as to the choice of apparatus. . . . If a worker submit voluntarily to examination, he will naturally ask that he and his family are not to suffer financially while he is undergoing treatment for what, in his opinion, might have healed at work. Tuberculosis is coming to be regarded more and more as a disease of economics; good food and freedom from worry about dependents are essential concomitants of cure. The real problem is to avoid victimization of the worker; a government subsidy is an inevitable corollary to large-scale mass radiography'.

As to the effect of the increased propaganda and the improved facilities for diagnosis at tuberculosis dispensaries recent figures are not encouraging. Wing-Commander Trail, of the Surgical Unit, Papworth, in the very last number of the *Lancet*, tells us that in 1927, of adult patients admitted to residential treatment for pulmonary tuberculosis under the L.C.C. scheme, only 6 per cent were classified as B. 1 at the time of admission, and 78.4 per cent as B. 2 or B. 3. In 1937, that is ten years later, 5.7 per cent were B. 1 and 80.3 per cent B. 2 or B. 3. Evidently no improvement toward earlier diagnosis was made in ten years. Can we wonder that so 'few survive for five years after discharge from sanatorium treatment?' Patients discharged in 1932 from L.C.C. residential institutions and traced till 1937 give the following survival rates: For B. 2 cases 41.2 per cent; for B. 3 cases 7.9 per cent; the survival rates for B. 1 cases being 81 per cent. These are the kind of facts which were established before the Dawson Committee was appointed. They have for some time been accepted as proved by practically everyone directly concerned with the tuberculosis problem. They are all taken into account in the small pamphlet (issued by H. M. Stationery Office and sold for 9d.) embodying the Report of the Commission on Tuberculosis in Wartime, and in it the practical measures thought necessary are summarized with directness and sufficient particularity.

This problem of diagnosis at a stage early enough to ensure that the chances of healing are reasonably good is one which has received relatively little attention in this country. In our last tuberculosis number we published an article, again by Dr. Benjamin, in which poor survival rates were recorded even after the best sanatorium treatment. In other countries, mass miniature radiography is being increasingly relied on to solve this problem of early diagnosis.

In most recent writings on the control of tuberculosis the importance of segregation of open cases of tuberculosis from children and young people is strongly emphasized.

Our present issue contains an article on this subject by Dr. R. Ali Shah. He points out that the importance of isolation was stressed by Sir Arthur Newsholme over 30 years ago, that in recent years much information on this subject has been presented, and that the isolation of the open case is accepted as a policy of anti-tuberculosis work in most countries. One urgent problem of tuberculosis work in India would appear to be that of prevention of the open cases of tuberculosis infecting others, particularly children and young people.

All the points here discussed endorse the plea of Dr. Benjamin that the development of anti-tuberculosis work should be carefully planned along sound lines, and be gradually developed along these lines.

In this tuberculosis number we have an article by T. J. Joseph, on 'War and Tuberculosis'. There is little doubt that the war will accentuate the tuberculosis problem in India as it has already that of other countries, and it seems more than probable that quite a marked increase in tuberculosis is occurring or will occur. The migration of larger numbers of people from one part of the country to another, the abnormal living conditions often prevailing in the war-affected areas, the increase in malnutrition and actual starvation now being seen in some parts of India are bound to produce an increase in tuberculosis.

J. L.

Medical News

IN MEMORIAM JAMES CARSON (1772-1843)

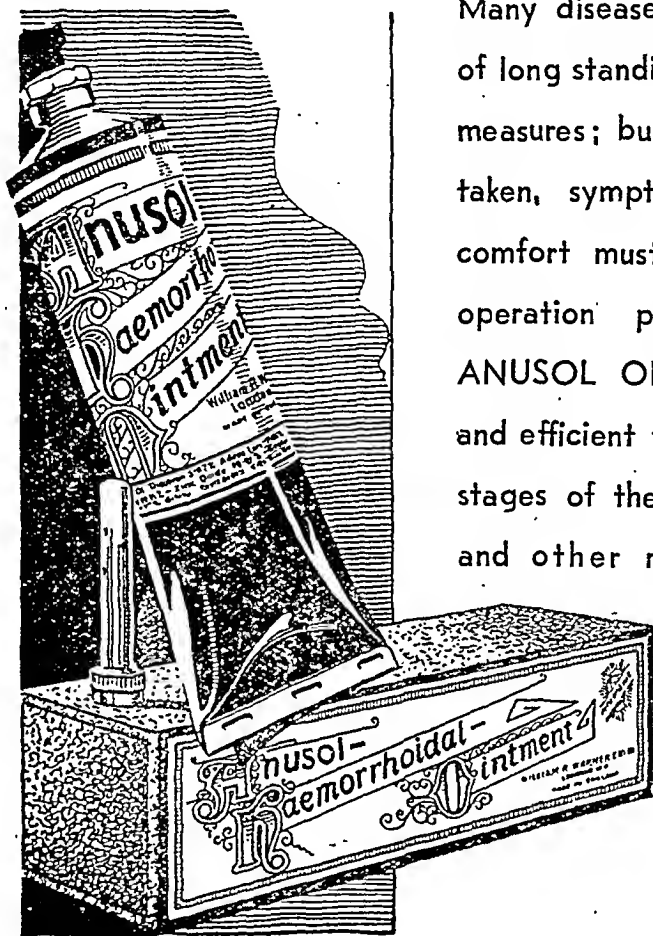
By K. EISENSTAEDT, M.D., T.D.D.
Jamnagar

It seems to be opportune to remember in this year's Special Tuberculosis Number, the centenary of the death of *James Carson*, the most prominent forerunner of the much celebrated Forlanini. He was the first clearly to point out the theoretical basis of modern collapse therapy of tuberculosis.

In 1819, he published his first paper 'On the elasticity of the lung'. Further experimental work on animals, including induced pneumothorax, prompted him to submit his physiological experiences to practical application. In his communications, 'The lesions of the lung' (1821) and 'Essays, physiological and practical' (1822), he was the first, indeed, who inaugurated in a scientific way the use of pulmonary collapse for treatment of lung tuberculosis, sixty years ahead of Forlanini. Although his work was known to many of his contemporaries and to some later scientists, it fell into oblivion, so much so that his name and work were unknown even to Forlanini. Long after the latter's method was well established, the importance of Carson's statements was remembered by Daus (1909), and his work is now fairly dealt with wherever a historical review of collapse therapy is undertaken, e.g. by Archibald, Brown (1941), Davies (1933), Fishberg (1932), Rubin (1937), etc. His perspicacity and almost prophetic outlook is best shown in his own words:—

'The chief cause of the peculiar obstinacy observed in the healing of injuries of the lungs arises, in my opinion, from the state in which the substance of these organs is held in the living system. It has been proved that the substance of the lungs is powerfully elastic, and that in the living system it is at all times

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on the stretch. When a lesion from any cause occurs in the lungs the sides of the divided substance recede in opposite directions; and a power equal to the elastic spring of the fibres tends, not only to prevent the approach of the sides of divided parts, but still farther to increase the breach. . . .

'There can be no doubt, however, that one of the lungs of an animal may be reduced to a state of collapse with perfect impunity. . . .

'This might be accomplished by admitting a small quantity of air into the cavity of the chest at one time, and allowing an interval to exist between the successive admissions, which may be necessary before the lungs shall be brought to a state of complete collapse. . . .

. . . . It has long been my opinion that if ever this disease is to be cured, and it is an event of which I am by no means disposed to despair, it must be accomplished by mechanical means, or in other words by a surgical operation. Whether the method proposed will be found practicable, or, if practicable, to the desired extent beneficial, or whether, as will be supposed by far the most probable, it may amuse for a moment and then like all its predecessors sink into deserved neglect, are questions which must be left to the decision of time. Whatever may be the event, I shall have this consolation, that I incur no risk in this case, by any proposition that may be made, of diverting the current of inquiry into a channel that shall be less productive than any of those in which it has hitherto run.'

To quote Brown (1941), 'James Carson (1772-1843), a Scot, was first educated for the ministry but was later graduated in medicine at the University of Edinburgh in 1799. He lived and practised in Liverpool. In 1837 he was elected to the Royal Society'. His own attempts, in 1822, to have artificial pneumothorax induced in two cases by the surgeon Bickersteth of Liverpool, were unfortunately unsuccessful. This fact does not lessen the importance of his work which places him among the great men in history of medicine.

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NEW STANDARD FOR PITUITARY EXTRACT: IMPORTANCE TO INDIAN MANUFACTURERS

THE new standard for Pituitary Extract set up by the National Institute for Medical Research (Great Britain) on behalf of the League of Nations has also been adopted for India by the Biochemical Standardization Laboratory.

Posterior Pituitary Extract, taken from the posterior lobe of the pituitary glands of mammals, is a most important medicinal agent in gland therapy. It is used to contract the uterus after childbirth and, as a cure for the effects of shock, for certain toxic cases and for a particular type of diabetes. Once entirely imported, it is now manufactured in large quantities in many centres in India and its standardization is a difficult matter. The League of Nations Health Organization set up a standard, internationally adopted in October 1935, and the Biochemical Standardization Laboratory was authorized to distribute it free to manufacturers in India.

When supplies of the old standard were exhausted the new one was set up which is approximately 15 per cent more potent. Its adoption for India makes it strongly advisable that manufacturers of pituitary extract preparations should adapt their products accordingly and the Biochemical Standardization Laboratory at Calcutta are willing to help by giving information or samples of the new standard.

ALL-INDIA MEDICAL CONFERENCE

THE following resolution was passed by the XIX All-India Medical Conference held at Patna during the last Easter holidays:—

'In order to stimulate intensive study and research on puerperal sepsis the control of which is of vital importance to the nation, this Conference recommends to various medical institutions in the country to undertake detailed investigations of this disease in its different aspects, bacteriological and clinical, and to make available to the profession their findings in this respect. This Conference recommends to the Indian Medical Association to offer a medal or prize for the best paper on the subject to be read at the next session of the All-India Medical Conference.'

Dr. K. S. Ray, an Ex-President of the Indian Medical Association, has offered a Gold Medal for the best paper on the subject to be read at the next session of the Conference to be held at Ahmedabad during the ensuing Christmas holidays. The last date for receipt of papers will be notified later.

P. B. MUKERJI,

*Honorary General Secretary,
Indian Medical Association,
12, Hindustan Buildings,
Calcutta*

ALL-INDIA MEDICAL CONFERENCE AHMEDABAD

THE Local Branch of the Indian Medical Association has invited the All-India Medical Association to hold their next Annual Session at Ahmedabad during Xmas week this year.

The Conference discusses subjects of professional interest in its scientific, social and economic bearings and records its decisions in resolutions, which, by reason of their being the resolutions of the largest professional organization in the country, command prestige and status in all matters—medical.

The communication may be addressed to The Secretary, Publicity Section of the 20th All-India Medical Conference, Ahmedabad.

Current Topics

Early Diagnosis of Pulmonary Tuberculosis

By R. R. TRAIL

(Abstracted from the *Lancet*, Vol. II, 10th October, 1942, p. 413, in *British Medical Bulletin*, Vol. I, April 1943, p. 22)

THE author of this paper is Physician to the Royal Chest Hospital (London) and to the Surgical Unit at Papworth Settlement. He points out that, in spite of the technical advances of recent years, there is much to be done before the diagnosis of early pulmonary tuberculosis is achieved. Increased propaganda and improved dispensary facilities for diagnosis have not materially affected the stage at which the disease is diagnosed, and the majority of sufferers are therefore still unsuitable for modern methods of treatment.

The principal cause of the failure to diagnose tuberculosis at the early stage is that the doctor has had to wait until the patient consults him over symptoms, whereas it is well known that many cases of established phthisis are symptomless. However, there is

sometimes a failure to diagnose tuberculosis when warning signs are manifest. These include pleurisy, persistent cough, indigestion, lassitude, fistula-in-ano, amenorrhoea and erythema nodosum. Similarly, there are physical signs present long before adventitious sounds are heard, for example, the sternomastoid sign (tension of the homolateral sternomastoid muscle at its origin at the proximal extremity of the clavicle) and lack of movement. Careful physical examination may show that cases considered bronchitic are, from stethoscopy alone, clearly suffering from early active tuberculosis.

Aids to diagnosis are the erythrocyte sedimentation rate, exercise tests and sputum tests, but radiological examination in the hands of a chest physician or radiologist with specialized chest training is much superior to any other method. Radiography is a method which, even at its lowest valuation, is a visual indication calling for immediate and strict doctor can seek out the patient by this means, as proved by the growing experience of the examination of the supposedly healthy.

The author reviews the results in 30,000 men and 10,000 women in the Royal Air Force examined by mass radiography, using 35 mm. units. In this series the incidence of active tuberculosis was 0.22 per cent for men and 0.33 per cent for women. The figures for inactive tuberculosis were respectively 0.36 per cent and 0.56 per cent. The incidence of active disease was about 1 per 1,000 more for women than for men at the age group 20 to 24, while the incidence for women under 20 was more than double that for men. Similarly, for inactive cases, the incidence in women under 20 was four times as great as among men, and one and a half times as great in the age group 20 to 24. The percentages approximate in the age group 25 to 29. On the basis of the results obtained by this survey, the author estimates that there may be in Britain 15,000 cases of active pulmonary tuberculosis among the supposedly healthy in the age group 18 to 24 years.

Experience shows that some 25 per cent more cases are found in the early stage of disease by mass radiography than by present civilian methods of diagnosis. While one radiographic examination is useful, it is no guarantee for the future and periodic examinations are desirable.

The author concludes with the recommendation that routine mass radiography of the civil population should begin at school-leaving age and be repeated annually until the age of 30 or 35 is reached.

A Preliminary Note on the Complement Fixation Test for Amoebiasis with Antigens prepared from *Entamoeba histolytica* grown with a Single Species of Bacteria

By C. W. REES
J. BOZICEVICH
L. V. REARDON
and
F. JONES

(Abstracted from the *American Journal of Tropical Medicine*, Vol. XXII, November 1942, p. 581)

The number of cases represented in our preliminary series is admittedly very small and general conclusions cannot be drawn until an adequate number of tests can be carried out under controlled conditions. However it would appear from these initial results that the *E. histolytica* organism antigen possesses a marked specificity and a high degree of potency. It is worthy of note also that relatively high dilutions of antigen and serum and large amounts of complement were used in our tests with the consequent minimizing of sources of error inherent in tests with concentrated materials. No doubt further improvements can be effected in the method of cultivation and richer harvests of amoebae may yield concentrates of even greater antigenic potency.

The Use of Sulphaguanidine in the Treatment of Dysentery Carriers

By L. A. RANTZ
and

W. M. M. KIRBY

(Abstracted in the *Bulletin of Hygiene*, Vol. XVII, September 1942, p. 620, from the *Journ. Amer. Med. Assoc.*, Vol. CXVIII, 1942, p. 1268)

ELEVEN hospital employees were treated, from whose stools dysentery bacilli had been isolated. In most cases the organisms had the characteristics of *Shigella alkalescens* (an organism which is not identified sufficiently often). About half the patients had had mild gastro-intestinal symptoms. Each patient was given 12 gm. of sulphaguanidine daily for two to six days, the total dose ranging between 16 and 84 gm. One man gave up the treatment because of vomiting, but toxic manifestations were rare and the men all continued at work. In nine cases all dysentery bacilli disappeared from the stools, but the other two cases remained carriers after three courses of treatment. The method would seem to have great possibilities for the control of outbreaks of dysentery in the armed forces.

Sterilization of Sulphanilamide Powder

(From the *Medical Press and Circular*, Vol. CCIX, 17th February, 1943, p. 98)

THE possibility that tetanus may be conveyed by sulphanilamide powder, or the containers in which it is kept, has recently aroused attention and the Medical Research Council, together with the Association of British Chemical Manufacturers, have therefore investigated the matter with a view to evolving a method for sterilization. The way in which existing stocks could also be sterilized was further considered. The following procedures were recommended for small-scale sterilization of powder in hospitals, etc.:

(a) *Dry heat maintained at 150°C. for one hour in a paraffin bath*, with the technique proposed by H. Berry (*Pharmaceutical Journal*, 1942, 24th October, 139) as follows: 'Use dry sterile cotton-wool plugged test tubes (5 in. by 3 in. or smaller diameter). Half fill them with the dry powdered substance, using a powder funnel. Flame the upper portion of the tubes and replug with the sterile plugs. Immerse to within one inch of the tops of the tubes in a liquid paraffin oil bath and maintain at 150°C. for one hour. If the tubes are to be stored the plugs should be covered with cellophane or paper.'

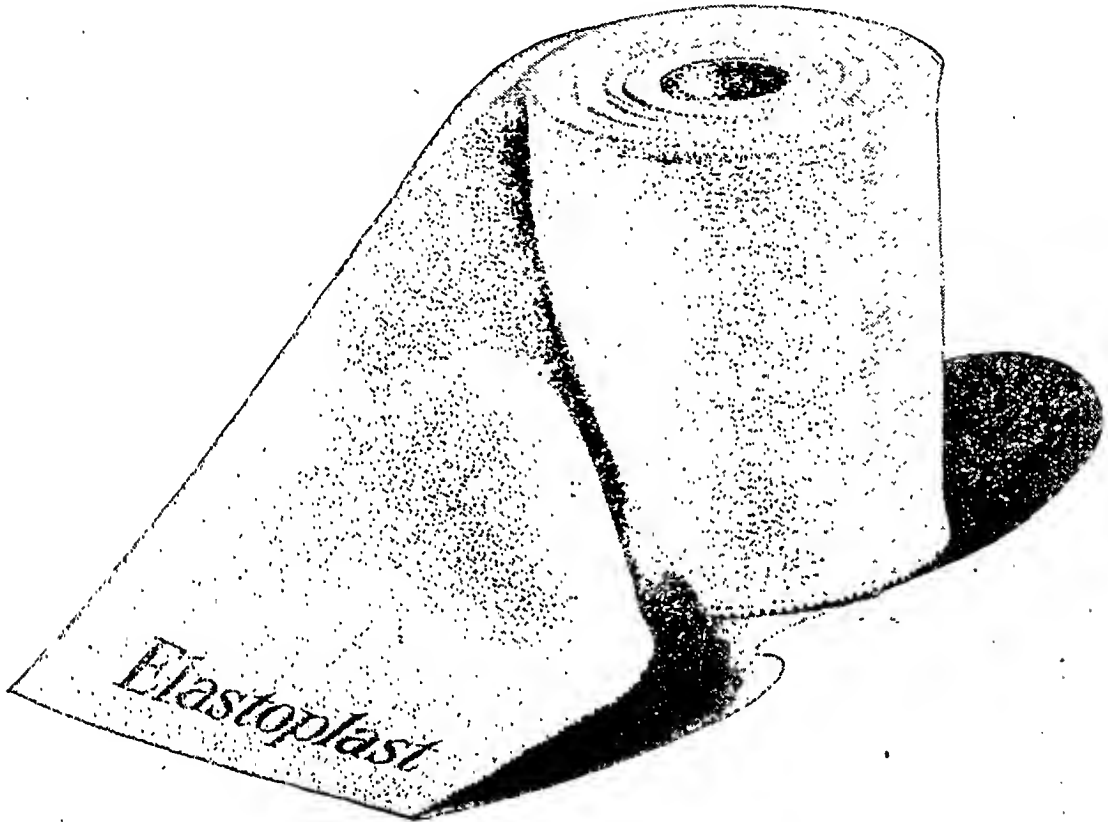
(b) *Dry heat maintained at 150°C. for one hour in an electric oven*, with precautions to ensure even heating throughout.

(c) *Autoclaving in a dressing sterilizer* by the technique and with the precautions proposed by W. J. Buckland (*British Medical Journal*, 1942, 29th August, 264), as follows: An autoclave with vacuum drying attachment (dressing sterilizer) is used and the container is a dry boiling tube plugged with a non-absorbent wool. 'The boiling tube must be thoroughly dried, if possible in a hot-air oven. (1) The jacket pressure of the sterilizer should be ready at a pressure of 20 to 30 lb. (2) Allow steam at 20 lb. into the empty closed chamber of the autoclave and leave for five minutes. (3) Using the appropriate valves clear chamber of all steam and condensed water. This process has heated the chamber and the boiling tubes loosely plugged with non-absorbent wool and containing the powder (in 5- or 10-gramme batches) are now placed in it. They should be placed on their sides, with the powder spread over their full length, giving a thinner mass for the steam to penetrate. (4) Leave the tubes for fifteen minutes in the hot chamber; this heats tubes and contents sufficiently to prevent condensation inside and on the powder. (5) Autoclave at 15 lb. for half an hour. (6) Clear the chamber of

E. B. 9

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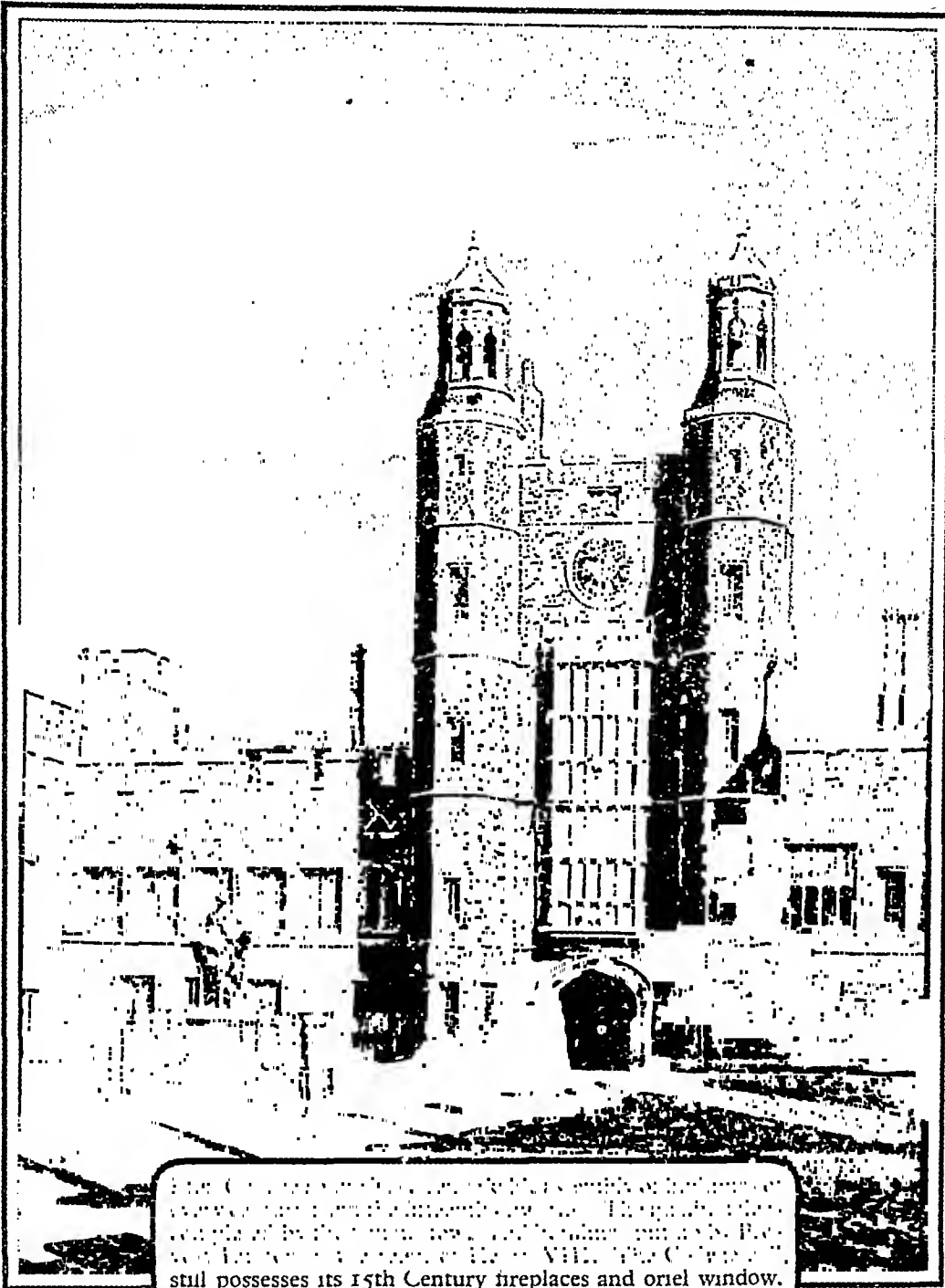
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steam and any condensed water quickly, and allow vacuum of 10 to 15 inches for fifteen minutes. (7) Remove tubes from autoclave, place a tight sterile plug of non-absorbent wool on the top of the one already in, and cap tubes with a suitable paper—preferably cellophane. Caking does not occur. If apparent caking is present while the powder is still hot, and when cool, a tap on the side of the tube is all that is necessary to show the sterile preparation to be the desired soft powder.

A proviso should be added with each of these recommendations that a sulphanilamide powder to be satisfactory for local application should not cake nor be more than slightly discoloured with any of the techniques proposed.

The recommendations of the conference related only to sulphanilamide powder, as the sulphonamide preparation most frequently applied locally. It may be mentioned, however, that the paraffin bath technique described by Berry (above) is recommended by the author as being suitable also for the sterilization of sulphathiazole powder in hospital practice.

Abstracts from Reports

ANTI-TUBERCULOSIS CAMPAIGN IN HYDERABAD-DECCAN. BY H. HYDER ALI KHAN, F.R.C.S.E., DIRECTOR, MEDICAL AND PUBLIC HEALTH DEPARTMENT, H.E.H. THE NIZAM'S GOVERNMENT, HYDERABAD-DECCAN, 1943

Dr. H. Hyder Ali Khan, F.R.C.S.E., Director, Medical and Public Health Department, H.E.H. The Nizam's Government, has sent us an interesting report on the above subject. This report is summarized here:—

The idea of providing special facilities for tuberculous patients originated from H.E.H. The Nizam nearly 18 years ago and a scheme was submitted to Government in 1930 including provision of clinics, hospitals and sanatorium. The final plans were sanctioned and the work started in 1937.

INCIDENCE AND MORTALITY

It is estimated that the total number of active tuberculosis cases in the State is not less than three lacs and that at least 30,000 persons die every year. The attendance of tuberculous patients in hospitals and dispensaries is fairly large but has markedly declined during the last 5 years, as shown by the following figures. For these facts Dr. Khan offers no explanation.

1937-38	29,361
1938-39	21,705
1939-40	16,449
1940-41	15,624
1941-42	11,435

The disease is fairly common in Hyderabad City, and is believed to be more prevalent among the Moslems and the female sex.

CLINICS AND HOSPITALS

These are situated in and about the city. There is a Clinic at Dabirpura in a specially constructed new building well equipped with x-ray, laboratory, room for artificial pneumothorax, emergency beds, etc. This Clinic is also a centre for propaganda purpose and provides for the after-care and continuation of treatment of patients after discharge from hospitals. Clinics are also attached to the out-patient departments of the Osmania General and the Lingampalli Tuberculosis Hospitals. The former has, in addition, 40 beds for tuberculosis cases under the care of a highly qualified specialist. Surgical work is developing in this hospital. The hospital at Lingampalli has accommodation for 60 patients and is equipped with radiology and light treatment, laboratory, and facilities for modern treatment. Owing to congestion and unhealthiness of the

locality, it will be shifted to Iram Numa Palace which has been purchased, 6 miles from the city, and is capable of accommodating 200 beds. It is situated in a beautiful garden on spacious grounds measuring 61 acres and will include isolated buildings for those patients who 'will not come to the hospital without the relatives accompanying them'.

SANATORIUM

One is being built on the Ananthagiri Hills at Vicarabad, 2,303 feet above sea level, 50 miles from the city and accessible by train or bus. The average annual rainfall is 25 inches and the maximum temperature in hot weather ranges between 98°F. and 105°F.; the nights however are cool and pleasant. The minimum temperature in winter averages 75°F. to 85°F. About 143 acres of land have been acquired and it is intended to acquire the remaining part of the plateau for the 'after-treatment colony', etc. The work is progressing rapidly.

SLUM CLEARANCE

The Hyderabad City Improvement Board spends 5 lacs every year on clearing the slums, building pucca model houses and providing new dust-proof roads with drains, etc. It has spent so far Rs. 87,30,661 in opening and clearing 1,000 acres of slum area in the city and will clear a further 300 acres. Three thousand and nine hundred model dwellings of various types have been built at a total cost of 47 lacs of rupees, due regard being paid to light, ventilation, air space, cleanliness and sanitary arrangements. The rent of these houses is not higher than Rs. 20, some being as low as Re. 1. In these developed areas, parks, children's play grounds and gymnasiums have been provided. A special area in the town has been set apart for industrial purposes.

District Boards and Municipalities are also improving the bigger towns in consultation with the Public Health Department. Rural housing conditions are changing though slowly.

PROPAGANDA AND SURVEYS

The city tuberculosis scheme and propaganda work are being carried out by a specialist trained in England and on the continent. He has two assistant surgeons and three sub-assistant surgeons under him. Propaganda is carried on by means of leaflets, lantern lectures and cinema films. There is a cinema car for public health lectures and demonstrations. Domiciliary visits by doctors and health visitors are arranged. A tuberculin survey has recently been started and 4,932 cases have been x-rayed for early detection of the disease. House treatment is also organized but it has not proved a success.

It is the intention of the Medical Department to extend the anti-tuberculosis work to the rural areas and to the other towns as well. Action is already taken in this matter.

A Tuberculosis Association was inaugurated in May 1941.

H.E.H. The Nizam's Government and Dr. Khan are to be congratulated for the efforts they are making in tackling the tuberculosis problem.

Service Notes

APPOINTMENTS AND TRANSFERS

To be Honorary Surgeon

COLONEL (Actg. Brig.) W. ROSS STEWART, C.I.E., *vice* Brevet-Colonel (Local Brig.) B. C. Ashton, vacated. Dated 6th March, 1943.

Captain R. K. Garde, Deputy Assistant Director-General, Indian Medical Service (A.R.P. Medical Stores), is transferred as Additional Officer to Medical Store Depot, Bombay, with effect from 31st July, 1943.

LAND FORCES

INDIAN MEDICAL SERVICE—SECOND TO INDIAN ARMY
MEDICAL CORPS

(Emergency Commissions)

To be Captains

- Harry William George Williams. Dated 26th March, 1943.
 Subodh Kumar Chatterji. Dated 4th June, 1943.
 Nanigopal Sengupta. Dated 7th June, 1943.
 Surapati Mukerji. Dated 11th June, 1943.
 Mritunjoy Kumar De. Dated 1st July, 1943.
 Manindralal Biswas. Dated 5th July, 1943.
 Kharshedji Kavasji Patel. Dated 8th June, 1942.
 Pandurangarao Gopalrao Gollerkeri. Dated 7th June, 1943.
 Gobichettipalayam Kuppuswami Iyer Venkataraman. Dated 10th June, 1943.
 Ashutosh Basu Sarbadhikary. Dated 7th July, 1943.

To be Lieutenants

- Dudley Clarence Wilkins. Dated 10th April, 1943.
 Daniel Fredrick O'Malley. Dated 7th May, 1943.
 Newton Braganza. Dated 5th July, 1943.
 Kenneth Morrison Herd. Dated 17th July, 1943.
 R. C. Hopkins-Husson. Dated 22nd December, 1942.
 Charles Joseph Hart. Dated 13th April, 1943.

(WOMEN'S BRANCH)

To be Captains

- (Miss) Malati Mallannah Shrinagesh. Dated 11th June, 1943.
 (Miss) Matilda Butt. Dated 18th June, 1943.
 (Miss) Jasmine Enoch. Dated 21st June, 1943.
 (Miss) Kootalathodi Gopalapanikker Janaki Bai. Dated 4th July, 1943.

To be Lieutenants

- (Miss) Catherine Beemer. Dated 21st June, 1943.
 (Miss) Tarjore Vaidyanathan Sitalakshmi. Dated 26th June, 1942.
 (Miss) Dorothy Balraj. Dated 1st July, 1943.
 The services of 2nd Lieutenant F. M. W. Harrison were placed at the disposal of the Supply Department for employment as Additional Officer in the Medical Stores Department, Bombay, with effect from the 31st December, 1941.

PROMOTIONS

INDIAN MEDICAL SERVICE—SECOND TO INDIAN ARMY
MEDICAL CORPS

Majors to be Lieutenant-Colonels

- S. Smyth. Dated 24th July, 1943.
 M. H. Wace. Dated 27th July, 1943.

LAND FORCES

INDIAN MEDICAL SERVICE—SECOND TO INDIAN ARMY
MEDICAL CORPS

(Emergency Commission)

Lieutenants to be Captains

- Mrs. E. M. Bowles (Nee'Morgan). Dated 21st February, 1943.
 A. R. Dutta. Dated 25th May, 1943.
 K. P. Roe. Dated 15th June, 1943.

2nd July, 1943

- M. Satyanarayana. A. Gopala Moorthi.
 T. P. Balakrishnan. Dated 3rd July, 1943.
 A. K. M. M. Rahman. Dated 4th July, 1943.
 H. S. Gill. Dated 6th July, 1943.

13th July, 1943

- A. Hamid. A. K. Dawn.
 W. U. Khan.

- S. C. Bhattacharyya. Dated 14th July, 1943.
 S. M. Bhattacharjee. Dated 15th July, 1943.
 V. Ekambaram. Dated 21st July, 1943.
 M. A. Urumese. Dated 24th July, 1943.
 N. A. Chandrasekharan. Dated 25th July, 1943.
 T. S. Ganapati. Dated 28th July, 1943.
 S. A. Mallick. Dated 30th July, 1943.

(WITHIN INDIAN LIMITS)

- P. C. D. Gupta. Dated 13th July, 1943.
 C. R. Iyengar. Dated 16th July, 1943.

(WOMEN'S BRANCH)

- (Miss) K. Issac. Dated 4th July, 1943.
 (Miss) L. M. D'Silva. Dated 16th July, 1943.
 (Miss) D. T. Dias. Dated 17th July, 1943.
 B. B. Dutta. Dated 1st August, 1943.
 N. Somaraju. Dated 4th August, 1943.

13th August, 1943

- S. A. Majid. M. R. Reddy.
 22nd August, 1943

- B. B. Bhadury. B. V. Rao.
 S. R. Khan. Dated 23rd August, 1943.
 W. A. Malik. Dated 26th August, 1943.
 A. K. Bhattacharya. Dated 28th August, 1943.
 E. E. LeFeuvre. Dated 5th April, 1943.

Lieutenant (on probation) to be Captain
(on probation)

- B. M. Saigal. Dated 21st November, 1941.

(WITHIN INDIAN LIMITS)

- B. N. Bhargava. Dated 30th August, 1943.

RETIREMENTS

- Colonel T. C. Boyd, R.H.S. Dated 9th August, 1943.
 Lieutenant-Colonel J. C. Bharucha. Dated 2nd June, 1943.

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Original Articles

PHENOMENON OF AUTO-AGGLUTINATION IN MAN AFTER SULPHAPYRIDINE*

By J. G. PAREKH, M.R.C.P.

Honorary Assistant Physician, Sir J. J. Hospital,
Bombay

AUTO-HÆMAGGLUTINATION, *i.e.* agglutination of a person's red corpuscles by his own plasma or serum, is a rare phenomenon. There are only a few cases recorded in the literature. Much of the information here given is quoted from Cohen and Jones.†

In animals this phenomenon is known to occur and is not so uncommon in them as in the humans. Klein (1902) first observed it in horses. Later, Landsteiner (1903) studied this phenomenon in greater detail. Ottenberg and Thalhimer (1915) observed it in a cat. It was experimentally produced in rabbits by Rous and Robertson (1918). They showed that experimental bleeding increases the agglutination if already present.

According to Whitby and Britton (1942) 'auto-agglutination is often well marked in hæmolytic icterus and other hæmolytic anæmias, it is a characteristic feature of paroxysmal hæmoglobinuria, and is occasionally found in Raynaud's disease (Benians and Feasby, 1941), severe anæmias, trypanosomiasis, spirillosis, myeloma and cirrhosis of liver. They also say that bacterial contamination of normal cells may result in their developing pan-agglutinating properties.

In human beings this phenomenon has been recorded in the following clinical conditions:—

1. Chronic mitral endocarditis with broncho-pneumonia. In this case it was present in the patient's daughter also (Clough and Richter, 1918).
2. During convalescence from pneumonia, this patient was treated with injections of his own blood (Claveaux and Sánchez, 1924).
3. Trypanosomiasis—clinical and experimental (Kanthack *et al.*, 1898; Christy, 1904; Dutton and Todd, 1905; Lebœuf and Roubaud, 1906-8; York, 1911, etc.).
4. Cirrhosis of the liver (Reitmann, 1890; Klein, 1902).
5. Relapsing fever—clinical and experimental (Todd, 1910; Nattan-Larrier, 1910).
6. Syphilis (Todd, 1910; Dudgeon, 1909).
7. Epilepsy—long standing (Dudgeon, 1909).
8. Certain forms of icterus due to hæmolysis (Martin and Dárre, 1909).
9. Anæmia—secondary, due to bleeding piles and associated with heart disease in a pregnant woman. The child did not show the same phenomenon (Kliger, 1922).
10. Pernicious anæmia—W.R. was positive (Cohen and Jones, 1924).
11. After sulphanilamide administration (Scott and Meerapfel, 1939).
12. Snake poisoning (echis variety).

I wish to report here a case showing auto-hæmagglutination following sulphapyridine administration.

Case report

H. A. M., Mohammedan male, aged 35 years, was admitted into Sir J. J. Hospital under the care of Colonel S. L. Bhatia, I.M.S.

The patient had had pain in the chest and cough with expectoration for 12 days prior to admission. The pain was worse on coughing. He had also had pain in the throat and hoarseness for four days. There had been fever for five days, it came with rigors and went with perspiration.

There was no history of hæmoptysis; there was a history of gonorrhœa and syphilis.

The patient looked well-built but poorly nourished and ill. There was generalized pallor, and a peculiar cough and hoarseness. There was no dyspnoea, no cyanosis, no icterus. The lymph glands were not palpable except the inguinal group. The tongue was pale and coated and the teeth dirty. The throat was clear. The liver and spleen were not palpable. Lungs—slight impairment of note and harsh breath sounds in the left infra-clavicular region and a few crepitations at the same place and at the bases. The circulatory, nervous and urinary systems were normal.

Blood examination showed a normocytic anæmia, leucocytosis and no malaria parasites.

The Wassermann reaction was doubtful (repeated later—negative). The Widal reaction, examination for malaria parasites and for trypanosomes gave negative results throughout.

On one occasion a few pus cells were found in the urine and on another occasion a staphylococcus was isolated from the urine. On one occasion pneumococci were cultured from the throat. X-ray examination revealed sinusitis.

Soon after admission the patient was given M.&B. 693. He received 12 tablets, and he vomited once. The next day his conjunctivæ and skin showed a yellowish tinge, and M.&B. 693 was omitted. The van den Bergh test showed an indirect positive reaction, and the icterus index was 15 units. Dr. Best, the house physician, brought to my notice the fact that, in spite of repeated efforts, the blood film could not be made, as the red cells were found to be clumped. Had it not been for this observation, the case would have been missed. At first the pipette and diluting fluid were suspected but repeated attempts with different apparatus were unsuccessful, whereas with the same apparatus and the same diluting fluid, cell counts of other patients could be made. The phenomenon of auto-hæmagglutination was thus suspected. A drop of blood on being received on a slide directly from the finger prick showed the phenomenon.

The jaundice steadily improved. Then there was epistaxis for four to five days. The lung signs disappeared after about three weeks. The voice also improved. The patient ran an intermittent temperature without rigors for about three weeks and then the temperature subsided. Once the temperature was down, the patient refused to stay longer and had to be discharged.

A further study of this rare condition of the phenomenon was desirable. It was found that a drop of the patient's oxalated blood when dropped in a test tube containing tap water produced a beautiful shower (the test was suggested by Prof. Gharpure), the clumped corpuscles sinking to the bottom without the immediate occurrence of hæmolysis: normal blood produces a cloud or smokiness due to hæmolysis. The serum and plasma of the patient were found to agglutinate corpuscles of all human groups and also sheep's corpuscles in the usual dilution. To find out whether the corpuscles were responsible for this phenomenon or the serum, the venous blood was withdrawn in a syringe containing 3.8 per cent citrate solution, and was centrifugalized. The corpuscles were washed with

* Paper read before a meeting of 'Teaching Pathologists'.

† Note.—Cohen and Jones' article is reprinted in our present issue (p. 564) and the whole subject of auto-hæmagglutination is discussed in an editorial (p. 551).—
EDITOR, I. M. G.

warm saline (37°C.). The washed corpuscles were then suspended in normal saline (2.5 per cent suspension). The patient's red cells were not agglutinated by normal sera of any group except of group A and group O.

These results gave the patient's group as B. The serum of the patient agglutinated corpuscles of the patient as well as those of all four groups. This shows that the serum, and not the corpuscles, were responsible for the auto-agglutination. The test was carried out at room temperature (24°C.).

Then we took the corpuscles of the patient and also those of groups AB, A, B, O (2.5 per cent suspension in normal saline) and mixed them with the serum of the patient in various dilutions, and looked for agglutination at 37°C. and at room temperature (24°C.) with the following results :—

serum was mixed with washed patient's corpuscles, the mixture (2.5 per cent cell suspension) was kept in an ice chest overnight; the next day the supernatant fluid was removed and this was mixed with a fresh cell suspension of the patient's corpuscles. No agglutination resulted. The supernatant fluid was also tested against corpuscles of groups A, B and O. Agglutination resulted in groups A and O, not in B. The patient's unmixd serum which was kept as a control still possessed agglutinating properties. This showed that the agglutinins are absorbable.

The sera of other patients receiving sulphanilamide in small or large quantities did not possess abnormal agglutinating properties. Sera mixed with 'bacteramide' 2.5 per cent solution showed no change in agglutinating power. Because of the red colour of the drug, macroscopic readings were difficult.

TABLE

Cells of group	AGGLUTINATION WITH PATIENT'S SERUM IN VARIOUS DILUTIONS									
	at 24°C.					at 37°C.				
	1/2	1/4	1/16	1/64	1/128	1/2	1/4	1/16	1/64	1/128
AB	+	+	+	+	+	+	+	+	—	—
A	+	+	+	+	±	+	+	±	—	—
B	+	+	+	+	±	+	±	—	—	—
O	+	+	±	—	—	—	—	—	—	—
Patient's group B	+	+	+	—	—	—	—	—	—	—

+ agglutination; ± weak agglutination; — no agglutination.

Agglutination started to occur as soon as the bloods were removed from the incubator. Agglutination could be made to disappear and reappear at will by altering the temperature; a lower temperature brought on agglutination and a higher temperature disappearance. This shows that the agglutinins were active only at low temperatures. It also shows that the process is a reversible one.

The agglutinating powers of the patient's serum were greater for cells of the normal members of his own group B than for his own corpuscles.

On one occasion on 5th January, 1941, the patient's serum was found not to agglutinate his own corpuscles, this fact suggesting that the process of auto-haemagglutination is not constant. On testing the serum the next day, the phenomenon was obvious again. It was also found that the agglutinating titre varied from time to time.*

Since the agglutinins appeared to be the nature of a cold agglutinin, the usual procedure was adopted for its absorption. The patient's

Discussion

The questions which arise and need elucidation are, why does auto-agglutination occur and how is it produced?

It is not due to a definite disease either of the blood-forming organs or of the other systems because it has been found in a variety of disease conditions which have nothing in common.

It has been of the commonest occurrence in experimental and clinical protozoal diseases such as trypanosomiasis, relapsing fever and syphilis. It would be of interest to know whether these pathogenic agents could be responsible for its production. It does not appear that it is directly or indirectly due to these pathogenic agents, because syphilis and other protozoal diseases are so common and yet the phenomenon is so rare. In our case there was a history of the patient having suffered from syphilis; the Wassermann reaction was however doubtful on one occasion and negative on the other; there were no clinical manifestations of syphilis. Nattān-Larrier (1910) has, however, shown that the phenomenon could be produced by experimental infection of rats with relapsing fever

* This manuscript included the results of studies of agglutination of the red cells of animals by the patient's serum. These have been omitted.—EDITOR.

With a more virulent strain the phenomenon would appear early and with a milder strain the serum possessed a lower agglutinating titre. The agglutination phenomenon was diminished two days before the crisis, reappeared in a low titre at each relapse and disappeared after the cure. It is not transmitted to the foetus.

Nierenstein (1908) ascribed it to increased acidity of the blood which occurs in trypanosomiasis.

One suggestion has been that since the phenomenon occurs outside the body at room temperature, the occurrence of hæmagglutination would stop bleeding from small wounds on the surface and thus prevent further impoverishment of blood in severe anæmias.

Repeated bleeding has been suggested by Rous and Robertson (1918) as a cause, but auto-hæmagglutination is seldom found in chronic hæmorrhagic anæmia. The phenomenon has been observed in cases of hæmolytic anæmia more than in any other condition except protozoal disease. It is possible that anæmia is related to this phenomenon. Agglutination of red cells is followed by hæmolysis; it is therefore probable that auto-agglutination precedes hæmolysis. Further observations are necessary to substantiate this statement. Agglutinins are more powerful in the cold; it has been suggested that this is why persons with paroxysmal hæmoglobinæmia get an attack on exposure to cold. In this condition it is possible that the lowering of temperature brings about agglutination, and the hæmolysis of the agglutinated corpuscles in the kidneys gives rise to hæmoglobinuria.

It has frequently been observed that reactions following blood transfusion are very common when transfusion has been performed in cases of hæmolytic anæmia. This fact further supports the argument that the blood of patients suffering from hæmolytic anæmia contains powerful agglutinins, and that the fresh blood is attacked by the agglutinins. Possibly even the hæmolysis seen in the ordinary course in these cases is due to auto-agglutination which results in hæmolysis. Further proof is needed of this.

A case of auto-agglutination with massive thrombosis in venules due to snake poisoning (echis) has been reported. Hæmolysis has often been reported after snake poisoning. In these cases it is probable that agglutination may precede actual hæmolysis.

Recently Scott and Meerapfel (1939) recorded two cases in which the serum of the patients was so altered by the long-continued use of 'uleron' and sulphanilamide, and that corpuscles of all four groups were agglutinated. In one of these cases, on one occasion, the serum of the patient had agglutinated her own cells after they had been washed in citrated saline solution. This patient also suffered from agranulocytosis. These changes were only temporary.

In our case also, sulphapyridine administration for only one day (12 tablets, of which two were

vomited) was followed by the occurrence of auto-hæmagglutination. All patients receiving the sulphonamide group of drugs do not show this change. Its occurrence after the administration of the sulphonamide group of drugs is rare.

Scott and Meerapfel (1939) also found that normal serum treated for some considerable time (4 days or more) with sulphanilamide in a concentration of about 2.5 per cent appeared to agglutinate cells of any group. We repeated the experiment but without observing a similar change.

However, the above observations suggest that the sulphonamides may cause some alteration in the serum which makes it agglutinate its own corpuscles as well as the corpuscles of other patients.

In our case there was an associated hæmolytic jaundice. This supports the idea that agglutination was followed by hæmolysis and jaundice. It is probable that protozoal diseases, drugs or other infections produce some alteration in the serum which causes agglutination and this in many cases results in hæmolysis and hæmolytic jaundice.

Another explanation offered of its association with anæmia is that it is due to the inoculation of the animal with products of red cell breakdown. It has been observed in a case of pneumonia treated with auto-hæmotherapy. This explanation, however, does not hold good because it cannot be produced experimentally by the repeated injection in animals of their own red cells.

Transfusion of auto-agglutinating blood is not advisable if done at a rapid rate because these clumped red cells may act as multiple emboli. Moreover, hæmolysis of these corpuscles is likely to occur. If, however, the transfusion is done after warming the blood to 37°C. and is given slowly, no harm is likely to occur, because the agglutination phenomenon is in abeyance at this temperature. Nevertheless, in spite of all precautions, minor reactions are likely to occur.

Summary and conclusions

1. A case of respiratory infection treated with sulphapyridine and showing the phenomenon of auto-hæmagglutination has been described.
2. Clinical conditions in which it has been recorded in the literature have been mentioned.
3. The agglutination was most marked in the cold and was feeble or inactive at 37°C.
4. The process of auto-agglutination is not constant and is reversible.
5. It is shown that agglutinins could be absorbed.

I have great pleasure in thanking Colonel S. L. Bhatia, I.M.S., for permission to investigate and publish this case under his charge.

I also wish to thank Professor P. V. Gharpure and Dr. K. D. Monohar for helping me in the laboratory work.

position; lens—traumatic cataract; vision—finger movements. On the day of admission, excision of the prolapsed iris was done. X-ray localization with a contact lens showed the foreign body to be lying in the vitreous at a distance of 9 mm. from the centre of the cornea, a little below the centre (see figures 4 and 5, plate XXVII). On 4th February, 1943, under local anaesthesia, the foreign body was removed by the anterior route with the help of the Mellinger magnet. The foreign body was 7 mm. long.

Case 4.—Sgt. C. I., British soldier, aged 20 years, admitted on 1st March, 1943, with a history of injury to the right eye with a chip of iron on 19th February, 1943, while he was hammering. He had an iris prolapse excised on the day of the accident in a military hospital. On examination: small sclero-corneal wound at the 7 o'clock position; tension normal; pupil dilated and adherent to the wound; lens—traumatic cataract; vision—finger movements. X-ray localization with a contact lens showed the foreign body to be lying in the vitreous just behind and a little below the lens at a distance of 7 mm. from the centre of the cornea (see figures 6 and 7, plate XXVII). On the day of admission under local anaesthesia, the original wound was opened up by a keratome incision, and the foreign body was removed with the help of the Mellinger magnet. The size of the foreign body was 4 mm.

Case 5.—R. A., British soldier, aged 31 years, was admitted on 11th March, 1943, with a history of injury to both eyes 4 days before due to bursting of a hand grenade in front of him. On admission, both eyes had perforating injuries, with early signs of irido-cyclitis in the left eye. Both eyes had traumatic cataract. The tension in the right eye was normal, but in the left eye raised. The right eye had good perception and projection of light, but in the left eye there was only faint perception of light. X-ray localization with a contact lens showed one small foreign body to be lying in the vitreous of the right eye at a distance of 13 mm. from the centre of the cornea. There was another small foreign body in the right orbit just below the supra-orbital ridge but 2 mm. outside the upper margin of the contact lens, and so not inside the eyeball. In the left eye the x-ray localization with a contact lens showed one larger foreign body to be lying in the lens matter at a distance of 4 mm. from the centre of the cornea (see figures 8 and 9, plate XXVIII). On the day of admission, under general anaesthesia, the right inferior rectus was divided between two sutures, and the eyeball was rotated upwards; the sclera was incised at the site of election and the foreign body was removed by the posterior route with the help of the Mellinger magnet. Then the original wound in the left eye was enlarged with a keratome, and the larger foreign body lying in the lens was removed without difficulty with the help of the Mellinger magnet. The foreign body removed from the right eye was 1 mm. long and the one removed from the left eye was 2 mm. long.

Case 6.—Fitter B. K., Hindu male, aged 30 years, was admitted on 29th March, 1943, with a history of injury to the left eye with a flying piece of steel while he was working with a hammer and chisel on 17th March, 1943. On examination: one small old vertical corneal wound at 7 o'clock position; tension normal; pupil half dilated and adherent to the corneal scar; lens—traumatic cataract; vision—finger movements. X-ray localization with a contact lens showed one small foreign body to be lying in the vitreous at a distance of 20 mm. from the centre of the cornea, a little below and inner to the centre (see figures 10 and 11, plate XXVIII). On 7th April, 1943, under local anaesthesia, the inferior rectus was divided between two sutures, the sclera was incised behind the equator at the site of election, and the foreign body was removed without difficulty. The foreign body was 3 mm. long.

Case 7.—M. D., Hindu male, aged 26 years, admitted on 4th June, 1943, with a history of injury to the left eye with a flying piece of iron on 2nd June, 1943. On examination: a small corneal wound of 1 mm. size on

REPORT ON TROPICAL ULCERS

By D. R. BHARUCHA, F.R.C.S. (Eng.)

MAJOR, I.A.M.C.

Officer in charge, Surgical Division of an I. G. H. (I. T.)

THIS is a report on a series of 179 patients admitted to an Indian General Hospital between September 1942 and February 1943, suffering from ulcers of the skin. An investigation was carried out in order to find the cause of this extraordinarily large number of ulcers, and an attempt was made to shorten the stay of these patients in the hospital.

(Continued from previous column)

the lower part at 6 o'clock position; tension normal; pupil drawn downwards; lens—traumatic cataract; vision—finger movements only. X-ray localization with a contact lens showed a small foreign body to be lying in the vitreous at a distance of 23 mm. from the centre of the cornea and a little below the centre (see figures 12 and 13, plate XXVIII). On 18th June, 1943, under local anaesthesia, the inferior rectus muscle was divided between two sutures, the eyeball was rotated upwards, the sclera was incised at the site of election behind the equator, and the foreign body was removed without difficulty with the help of the Mellinger magnet. The size of the foreign body was 2 mm. X 1 mm.

Summary.—Intra-ocular eye injuries should be sent without delay for expert treatment. Localization with a contact lens is simple and efficient. Foreign bodies behind the lens are best taken out by the posterior route. Many intra-ocular foreign bodies are only slightly magnetic; therefore it is of great importance that the terminal of the magnet should be approximated to the foreign body; otherwise failure to remove it may result.

EXPLANATION OF PLATES XXVII AND XXVIII

- Fig. 2. Case 2.—Antero-posterior view. F.B. lying a little below and outside the centre of the orbit.
- Fig. 3. Case 2.—Lateral view. F.B. 6 mm. from the cornea.
- Fig. 4. Case 3.—Antero-posterior view. F.B. lying a little below the centre of the orbit.
- Fig. 5. Case 3.—Lateral view. F.B. 9 mm. from the cornea.
- Fig. 6. Case 4.—Antero-posterior view. F.B. lying a little below and outside the centre of the orbit.
- Fig. 7. Case 4.—Lateral view. F.B. 7 mm. from the cornea.
- Fig. 8. Case 5.—Antero-posterior view. Three F.Bs., two in right orbit smaller in the centre of the orbit, the other below the supra-orbital ridge. *Left eye.* One larger F.B. lying a little above the centre of the orbit.
- Fig. 9. Case 5.—Lateral view. Right eye. Three F.Bs., upper one outside the eyeball; 2nd, largest, 4 mm. from the left cornea; 3rd, smallest, 12 mm. from the right cornea.
- Fig. 10. Case 6.—Antero-posterior view. F.B. lying just below the centre of the orbit.
- Fig. 11. Case 6.—Lateral view. F.B. 20 mm. from the cornea.
- Fig. 12. Case 7.—Antero-posterior view. F.B. lying a little below the centre of the orbit.
- Fig. 13. Case 7.—Lateral view. F.B. 23 mm. from the cornea.

(Concluded at foot of next column)



Fig. 2. Case 2.

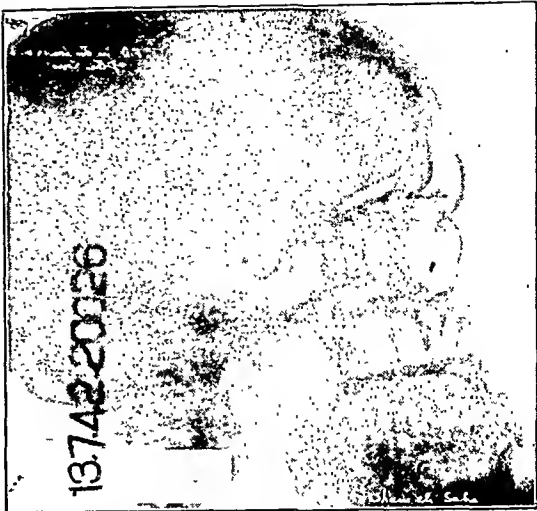


Fig. 3. Case 2.



Fig. 4. Case 3.



Fig. 5. Case 3.



Fig. 6. Case 4.

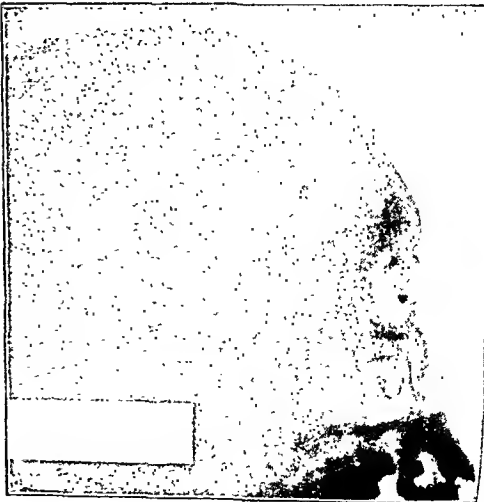


Fig. 7. Case 4.

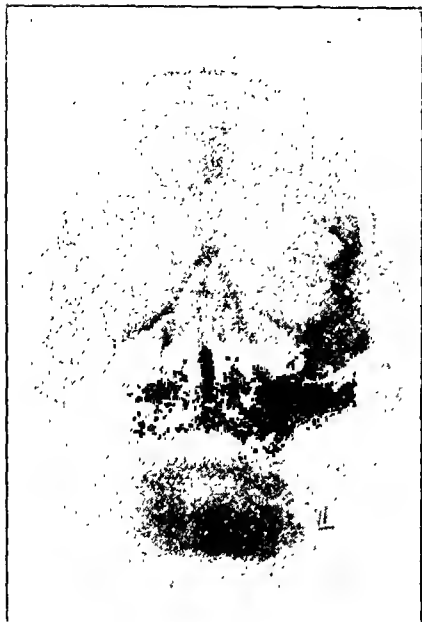


Fig. 8. Case 5.

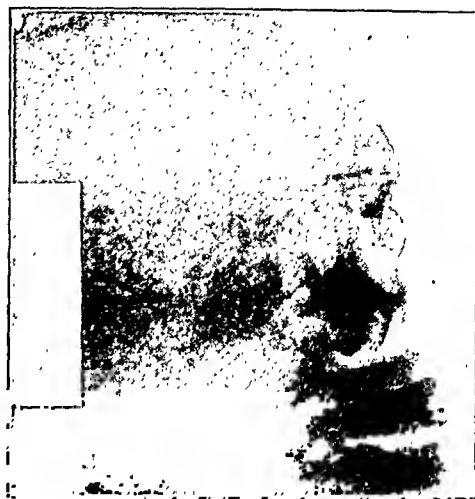


Fig. 9. Case 5.

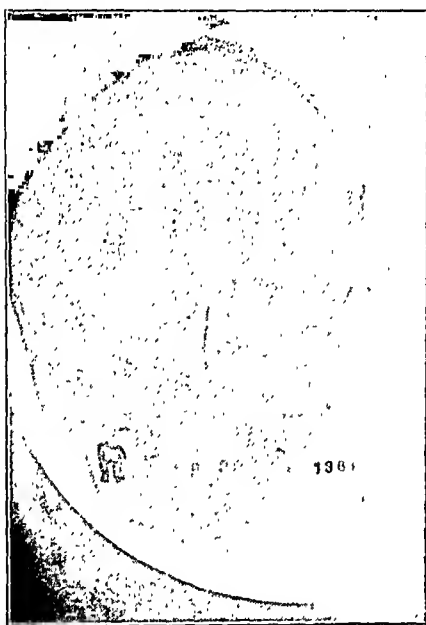


Fig. 10. Case 6.



Fig. 11. Case 6.

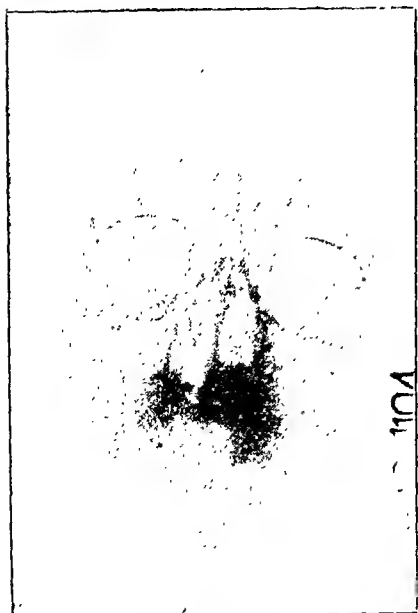


Fig. 12. Case 7.

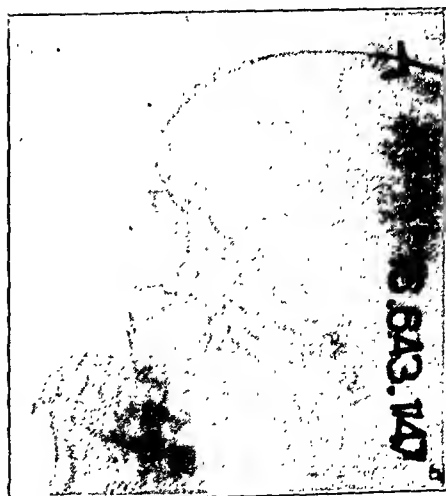


Fig. 13. Case 7.

The small foreign bodies are less easily seen in the photographs than in the original skiagrams.

Many theories have been brought forward by different investigators as to causation of these ulcers in the tropics. Poor diet, especially deficient in proteins, lack of calcium, lack of vitamins B and C, excessive humidity and excessive rainfall, specific organisms such as fusiform bacilli and a high incidence of syphilis have each in turn been labelled as the cause of these ulcers. We have made an attempt to investigate these causes and evaluate them.

Factors influencing the incidence

Locality of origin.—It is important to note that almost all of these patients came from a particular area.

Dates of admission.—The 179 cases of ulcers were admitted as follows:—

September 57, October 52, November 36, Total 145
December 19, January 13, February 2, Total 34

It will be noticed that 145 out of a total of 179 cases were admitted during the three months of September, October and November 1942 and only 34 cases in the next three months.

Relation to schemes of military training.—It is interesting to observe the point that very important, extensive, and strenuous military training schemes were carried out in this area from 26th September to 10th October, 1942, and from 31st October to 14th November, 1942.*

Relation to relative humidity and rainfall.—These in the area during the different months of the year are as follows:—

Months	Relative humidity, per cent	Rainfall, inches	Number of cases
September ..	61.3	6.03	57
October ..	79.6	9.87	52
November ..	73.2	6.64	36
December ..	83.0	17.87	19
January ..	76.9	5.81	13
February	2

It will be seen that both the relative humidity and the rainfall are the lowest during September and the highest during December, and yet the largest number of patients was admitted during September, and the admissions markedly fell off during December. This shows how little connection there is between the incidence of ulcers and relative humidity.

Relation to food. Calcium and vitamins B and C intake.—All our patients were Indian soldiers receiving a uniform diet as laid down by the Army authorities, which is known not to be deficient in any important dietetic factor.

<i>Relation to injury.</i> —Of the 179 patients, 160 gave a history of some form of injury or inflammation of the skin which preceded the ulcer. In most cases the nature of the injury was barbed wire, thorn, an insect bite, or an abrasion.		
Trauma	.. 134	
Boils	.. 24	
Burn	.. 1	
Leech bite	.. 1	
Not stated	.. 19	

Description of ulcers.—It is significant that 177 cases had ulcers below the level of the knee, that is on parts most exposed to injury.

The size of ulcers varied from $\frac{1}{2}$ inch to nearly 6 inches in diameter. The majority of ulcers were between $\frac{1}{2}$ inch to 2 inches in diameter. As will be seen from the following figures, the size of the ulcer bears a relation to the number of days after the receipt of the injury before admission. The figure for ulcers over 2 inches in diameter is not quite large enough to justify conclusions.

Diameter	Number of cases	Average number of days before admission
1 inch or less ..	87	16 $\frac{1}{2}$
1 inch to 2 inches ..	74	23
Over 2 inches ..	18	21

Most cases had one ulcer only, but some had as many as six. The shape of most ulcers was irregular, the margins clear cut. In the acute stage the surface was covered with a dirty yellowish-grey foul-smelling slough. The only tissues involved were the skin and the superficial fascia. The surrounding skin rarely showed any marked inflammatory reaction. The inguinal lymph glands were enlarged, painful and tender, the degree varying with the degree of inflammation. Almost all the patients complained of local pain and tenderness of the ulcer. A rise of temperature was rarely present.

Investigations.—The presence of other associated diseases and their effects on the ulcers were looked for, especially ankylostomiasis, dysentery, malaria, anaemia and avitaminosis. The last four were not present in an active form in this series of cases.

In addition the following routine investigations were made. Smears from the pus were made in all cases and examined after staining. Cultures were made from those cases which, when admitted, were in an acute stage. Neither of these methods showed the presence of any particular organism except staphylococci and diphtheroid bacilli.

I am informed that Captain Ratnavale examined 12 similar cases. He made smears from the floor of the ulcer after washing away the pus with saline, and found fusiform bacilli in the majority of his cases.

A routine stool examination showed that about 10 per cent of cases were suffering from

* The largest number of admissions was in the month of September. The intensive training starting on 26th September could hardly have a direct influence on this.—Editor, I. M. G.

ankylostomiasis but this had produced no appreciable effect on the hæmoglobin percentage or the R.B.C. count.

The urine was examined in all cases, and nothing abnormal was detected in any case.

The Wassermann and Kahn tests were done in 107 cases. Of these only 5 were positive.

Complications.—Not a single case showed any complication such as cellulitis or erysipelas. But a very interesting complication was noted in 13 of our cases. Not all of them were admitted to our hospital with acute ulcers, but 13 of the patients gave a definite history of a recent injury that had turned septic. These 13 cases developed a peculiar form of low-grade infection of the bone, affecting the periosteum and the cortex. All these cases showed both bone destruction and new-bone formation, a form of osteo-plastic periostitis. These 13 cases will be reported upon separately, and are only being mentioned here.

Treatment.—Two different forms of treatment were tried.

(i) This treatment was the one advocated by Vigors Earle of Trinidad. In short it consisted of (a) dressing ulcers daily with a solution of 1 in 150 copper sulphate till the slough completely disappeared, and (b) in the healing stage treating the ulcers with 40 per cent cod-liver oil in vaseline, and applying an occlusive elastoplast dressing, changed once in five to seven days. Ninety-two cases were treated by this method.

(ii) We were not quite satisfied with the results gained by the above method of treatment and adopted another suggested by Captain E. N.

dressing being changed once in three to five days as necessary. It should be pointed out that occlusive dressings with elastoplast was entirely given up as it was found to cause marked irritation of the surrounding skin in many of the cases, with the appearance of daughter ulcers.

Another point on which we lay emphasis is the rest given to the affected part. Except in the minor cases, all patients were strictly confined to bed with slight elevation of the affected part. It was not very easy to enforce this, and for many patients who did not obey this instruction, we were forced to tie back-splints with a foot piece to both the legs so as to make all movement out of the bed impossible. This was particularly necessary in cases of ulcers over the knee or the ankle. This form of enforced rest made a marked difference in the rapidity of healing.

When the second form of treatment was started we had 20 cases which had shown an extremely poor response to the first form of treatment. We therefore decided to try the second method in them too.

Finally there is a group of 67 cases in which only the second method of treatment was used.

The following table shows the average time each of these different groups of patients spent in the hospital. It also shows that the greater the delay in admission to the hospital, the bigger the size of the ulcer and a consequent longer stay in the hospital.

TABLE

Type of case	Number of cases	Average number of days after injury before admission to hospital	Average total stay in hospital in days	Average number of days on treatment II (in cases of B group)
A. Treatment I	Ulcer, 1 inch	51	17	35
	" 1-2 inches	34	21	46
	" 2 inches	7	23	54
	—	92		..
B. Treatment II. Persistent cases after treatment I.	Ulcer, 1 inch	12	16	48
	" 1-2 inches	6	21	67
	" 2 inches	2	19	26
	—	20		22
C. Treatment II only.	Ulcer, 1 inch	24	17	20
	" 1-2 inches	34	28	27
	" 2 inches	9	21	36
	—	67		..

Pearlman, I.M.S., and of which he had experience. Briefly it consisted of (a) dressing all cases in the acute stage with a powder of 50 per cent sulphonamide and 50 per cent iodoform, dressings to be changed every day, and (b) in the healing stage dressing with red lotion, the

It will be seen that the second form of treatment reduces the number of days spent in the hospital by about one-third to one-half.

Conclusion.—Weighing all the evidence at our disposal, we are forced to the conclusion that
(Concluded on opposite page)

SULPHONAMIDES IN UNDULANT FEVER

By P. N. BARDHAN, M.R.C.P. (Edin.), D.P.H. (Eng.)

MAJOR, I.M.S.

*From an Indian Field Laboratory in the M.E.F.**Introduction*

UNDULANT fever is an uncommon disease in India. Cases are occasionally reported, chiefly from institutions with laboratory facilities. One series of 13 cases was gathered by the late Lieut.-Colonel H. S. Rajan, I.M.S., at Lahore in

(Continued from previous page)

these so-called tropical ulcers have no specific causation of the nature of a special organism. From the evidence gathered here a few salient facts stand out. First, that almost all these cases came from one area only. Second, that 145 out of 179 cases were admitted during September, October and November 1942, when very extensive military exercises were being carried out in the area. Third, that out of 179 cases, 177 had ulcers below the level of the knee, i.e. over that part of the body most exposed to injury from barbed wire, thorns, etc. Fourth, that 160 cases gave a definite history of an injury or boil which started the ulcer. Fifth, that on an average from 15 to 27 days elapsed between the receipt of the injury and the admission of the patient to the hospital.

We are therefore forced to the conclusion that these ulcers started as small injuries which were neglected and became septic. Matters were made worse by the fact that many of these soldiers after the receipt of these minor injuries continued to take part in the training schemes, and they had to continue wearing boots and puttees and had few opportunities for cleaning the injured part or keeping it at rest.

It is not for us to ask here whether it is feasible that every soldier who receives any injury, however trivial, should have an opportunity to get the wound cleaned and dressed at the earliest possible moment, and be exempt from such duties as involve the constant use of the injured part till healing is complete. In the early stages of a minor injury, all that is required is cleanliness and rest to the injured part. Force is added to this suggestion when it is seen that these 179 patients spent in all 6,056 days in the hospital. This does not include the time before admission to the hospital during which they were not fit to work and the time spent by many of them at the convalescent depot.

It gives me great pleasure in thanking Lieut.-Colonel E. P. N. M. Early, I.M.S., officer commanding the hospital, for the encouragement and guidance given to me in carrying out this investigation. I also wish to thank Captain P. S. Rau, I.M.S., Captain M. J. Barry, I.M.S., Captain E. N. Pearlman, I.M.S., Captain M. M. Murray, R.A.M.C., and Captain J. R. Hewett, R.A.M.C., for their co-operation.

1930 (unpublished communication). The agglutination titre against the *Brucella melitensis* varied from 500 to 3,000. Treatment of these cases and other cases reported till then was essentially symptomatic and unsatisfactory. The position as regards treatment is unchanged to this day and is still unsatisfactory in that specific therapy is not available.

Literature

The advent of the sulphonamide group of drugs naturally led to their use in undulant fever, but the results have not been uniform. Manson-Bahr (1938) detailed the treatment in three cases of abortus undulant fever. Sulphanilamide was used after six weeks of illness in two and after four months in the other; 1.5 grammes of the drug were given daily by mouth, and this was successful in reducing the fever and the enlargement of the spleen. A relapse in one of the first two cases was treated successfully by subcutaneous injections of sulphanilamide. The author was satisfied that the effect of the drug in reducing the temperature was too striking to be merely a coincidence. Traut and Logan (1938) used the same drug in two cases. In the first the drug was used after failure of stock vaccines. The temperature fell after the second day, though the drug was continued for 9 days in all. In the second case, 30 grains of the sulphanilamide were used daily and the temperature fell after 48 hours. The cure, the authors imply, was permanent in both cases. In all the above five cases, diagnosis was confirmed by the agglutination tests.

Greig claims that 'the administration of sulphonamide-P (British Drug Houses) has been followed by satisfactory improvement. Two tablets of $7\frac{1}{2}$ grains each are given four hourly till 12 tablets in all have been taken'. He also claims safety, effectiveness, and tolerance for rubiazol in the melitensis type of undulant fever. Neumann (1938) treated a case in which fever abated in a week instead of months as is usual. Punch (1938), Thomson (1938), and Gaffney (1938) used sulphanilamide and prontosil and obtained favourable results. Morrison (1940) treated two cases of undulant fever successfully with sulphanilamide. He used 0.5 gramme four hourly for 10 days, the night doses having been omitted owing to some misunderstanding. In contrast to these results, however, Bynum (1939), using even larger doses, was unable to effect a cure in six cases.

A similar variation of results is reported in brucella infections in animals. Hamann and Huddleson (1939) gave 80 grains daily of sulphanilamide (about the maximum tolerated dose) to each of two infected cows with no evident improvement. On the other hand, Wilson and Maier (1939) succeeded in curing 8 infected guinea-pigs, though the dose required was very near the maximum tolerated. Similar cures in goats and guinea-pigs have been reported

by others (Welch, Wentworth and Mickle, 1938; Montgomerie, 1938; and Chinn, 1938).

Case reports

Personal experience with the use of sulphonamide in 3 cases of undulant fever, diagnosed both by positive blood culture and agglutination tests, is now described :—

The first case was diagnosed on the 17th day of the fever; prontosil album, 0.5 gramme, was given from the 18th day four hourly for 48 hours and 5.0 c.cm. of prontosil rubrum by intramuscular injection once a day for three days. It was thought that the injection of the first day would commence the bacteriostatic action while the oral dose was gathering momentum. Fever subsided on the 21st day, a few hours after the third injection; 0.5 gramme *t.i.d.* by mouth was continued for three more days. There was no fever from the 21st to the 37th day; it then recurred with rheumatic pain in both knees; immediately 0.5 gramme of prontosil album was given four hourly for 48 hours; this reduced the temperature but not to normal. As it appeared that the drug could not control the fever fully, it was discontinued, and symptomatic treatment followed. The case was finally discharged from the hospital on the 69th day rid of his fever, but anæmic and debilitated. During the next year and a half there was no relapse, and the general condition improved.

The second case was treated from the 23rd day by two intramuscular injections daily of 5.0 c.cm. of urea sulphazide (a sulphonamide preparation of Union Drug Co. of Calcutta). The fever came down to normal on the 26th morning, and one injection a day was continued for two more days. There was a small rise of fever for three days from the 35th to the 38th day, but the drug was not repeated.

The third case received an initial dose of 2 grammes of sulphanilamide followed by four-hourly doses of 1 gramme during the course of 4 days till a total of 26 grammes was given. The fever reached normal on the 42nd day but tended to swing between 98.2°F. to 99.6°F. for another 6 days. Only 0.5 gramme of the drug was given every four hours for 48 hours, and the fever subsided.

Assessment of results

The administration of the drug coincided with the remission of fever and abatement of other symptoms in two of the cases quoted above, and yet in the first the drug had no apparent effect. The result in this case is indefinite; had the drug been continued longer, an indication of its efficacy or otherwise could possibly have been obtained. The other two cases, however, were striking in that the drug controlled the fever and perhaps prevented relapses. The drug therefore seemed to have not only an antipyretic effect but it was also capable of cutting short the total course of the fever. However, success with one case each treated with urea

sulphazide and sulphanilamide is too little material to justify conclusions.

Mode of action

The exact nidus of *Brucella melitensis* during the apyrexial period is not known; the recurrence of the fever with joint pains is not altogether without significance. It is probable that even during the pyrexial bouts some of the organisms stay put in a nidus in such a manner that the sulphonamide drug cannot reach them in effective concentrations, thus explaining why one course of sulphonamide may not be curative.

The bouts of fever after treatment by sulphonamide in the above three cases were shorter and much less severe than would be expected in the natural run of the disease. The sulphonamide group is not bactericidal but only bacteriostatic. It is reasonable to argue that when the drug is discontinued, the organisms that have not been destroyed but have only been partly affected by the sulphonamide, come out into the circulation but with diminished virulence, and cause a recurrence of the fever which however is much less severe and of shorter duration. But for the bacteriostatic action of the sulphonamide, relapses of the usual severity and duration might reasonably have been expected.

It is now accepted that sulphanilamide acts by competing with *p*-amino benzoic acid for an enzyme that is essential for the growth of streptococci. A rational approach to treatment of undulant fever would therefore be firstly to study the metabolism of the causal organism, and secondly to synthesize a drug that would interfere effectively with the chain of events in the metabolism of the organism. This drug need not necessarily be of the sulphonamide series.

Summary

The position of the treatment of undulant fever is reviewed and its unsatisfactory state noted.

References are given bearing on experience with sulphonamide both in human beings and animals.

Details are given of three cases treated with sulphonamides, and the results obtained are assessed.

The possible mode of action of sulphonamide in undulant fever is discussed.

Acknowledgments

Thanks are due to Major B. I. S. Bhalla, I.M.S., for help with references, and to Captain M. Sanjiva Rao, I.M.S., for help in preparing the paper.

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OBSERVATIONS ON THE NEUROPATHIC SEQUEL OF DIAMIDINO-STILBENE THERAPY IN KALA-AZAR

By P. C. SEN GUPTA, M.B. (Cal.)

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Calcutta School of Tropical Medicine

DIAMIDINO-STILBENE is by far the most potent of the aromatic diamidines tested so far in the treatment of kala-azar. The immediate cure rate in Indian kala-azar is about 98 per cent, and the proportion of cases relapsing after a single course of treatment is very low. The use of this drug has however certain drawbacks. The intravenous injections are usually accompanied by certain unpleasant reactions. The immediate unpleasant reactions can be classed according to their degree of severity as *mild*, when there is burning sensation all over the body, flushing of face, slight giddiness; *moderate*, when the patient has more severe degree of the above symptoms plus vomiting, epigastric distress, dyspnoea, feebleness of pulse, sweating; and *severe*, when the patient has symptoms of collapse, with loss of pulse at the wrist. The causation of these symptoms has been discussed by Napier and Sen Gupta (1942). These immediate reactions however are not dangerous to life, though somewhat unpleasant to the patient, and can be prevented to a great extent and cured by adrenaline.

Certain more serious delayed toxic effects after the administration of diamidino-stilbene have been reported in recent years. The work of Devine (1938, 1940) in rabbits and Adler and Tchernomoretz (1939) in hamsters pointed towards a possibility of toxic action on the kidneys and liver. Kirk (Fulton and Yorke, 1942) stated that various toxic reactions had been observed in cases of Sudanese leishmaniasis treated with large doses of stilbamidine (diamidino-stilbene). Toxic reactions which developed some months after the disease had apparently been cured were serious; the patients suffered from vomiting and loss of weight, and some of them died with signs of hepatic failure. Kirk was of the opinion that these reactions were due to old solutions of diamidino-stilbene which had developed toxic properties. Delayed toxic affection of the liver has not been met with

so far in the large series of cases that has been treated by the workers of the School of Tropical Medicine in this country. This is probably because all these cases were treated with freshly prepared solutions of diamidino-stilbene.

Napier and the writer (Napier and Sen Gupta, *loc. cit.*) however described a peculiar neuropathic sequel to diamidino-stilbene therapy and reported seven cases. In the period that has elapsed since the publication of the above paper, ten more cases have come under observation, and in some cases it has been possible to follow up the course over a fairly long period. In this paper it is proposed to present the relevant data regarding this neuropathy in a tabular form, to analyse the symptomatology, and to discuss (i) the principal features of these cases, (ii) the site and the nature of the neurological lesion, (iii) the effect of the various therapeutic measures adopted to alleviate the symptoms and (iv) the prognosis of this condition.

Analysis of the data

Thirteen of the patients were Indians, two Europeans and two Anglo-Indians, 14 were males and 3 females. The age varied from 15 to 41 years. Six were 'resistant' cases of kala-azar and the rest (11 cases) were ordinary cases.*

Illustrative cases

The stippled areas correspond to the extent of dissociated anaesthesia, i.e. loss of sensation of light touch with preservation of sensation of pain, temperature and pressure.

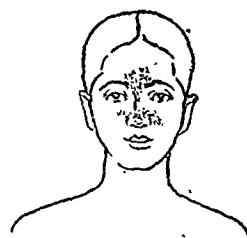


Fig. 1. Case 1.—Symptoms : numbness, partial loss of sensation, hyperaesthesia to temperature and touch.



Fig. 2. Case 2.—Symptoms : numbness, heaviness, blinking movements of the eyes, occasional twitching of some facial muscles.



Fig. 2a. Case 2.—Symptoms less severe, area affected less in extent.

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* Of total of 104 cases of kala-azar treated with diamidino-stilbene 88 were Indians, 2 Europeans, and 14 Anglo-Indians; 89 were males and 15 females; and 26 of the cases were 'resistant' and 78 ordinary cases of kala-azar. (For definition of 'resistant' case see Napier *et al.*, 1942.)

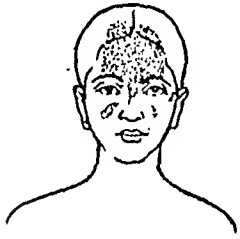


Fig. 3. Case 3.—Symptoms: troublesome formication, numbness.

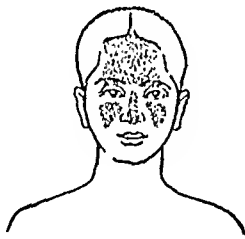


Fig. 3a. Case 3.—Symptoms less severe. Loss of pain sensation in areas marked with X.

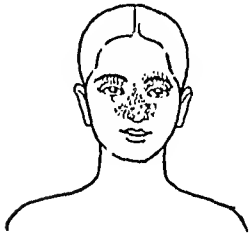


Fig. 4. Case 4.—Symptoms: numbness, impaired sensation, complete anaesthesia in area marked with X.

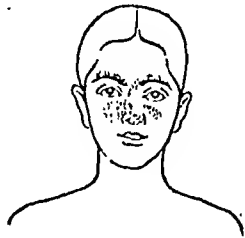


Fig. 4a. Case 4.—Symptoms worse, troublesome formication. Slight trophic changes over the eyebrows. Blinking movements of the eye.

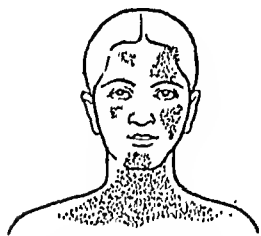


Fig. 5. Case 5.—Symptoms: heaviness and formication.

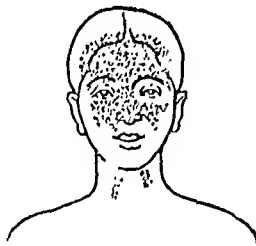


Fig. 5a. Case 5.—Symptoms: troublesome formication and itching. Pigmentation and roughness of affected area. Eyebrows stunted in growth and partly rubbed off. Blinking movement of the eyes.

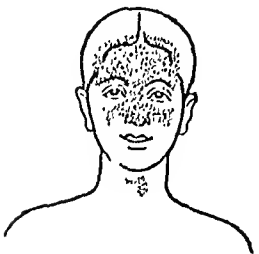


Fig. 5b. Case 5.—Symptoms less severe. Eyebrows have grown to normal.

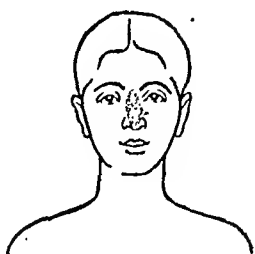


Fig. 6. Case 6.—Symptoms: numbness, stiffness and diminished sensibility.

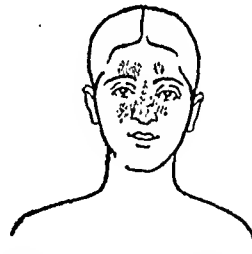


Fig. 7. Case 7.—Symptoms: loss of sensation, heaviness, uncomfortable itchiness.

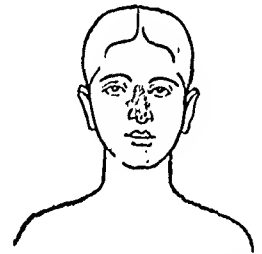


Fig. 8. Case 8.—Symptoms: numbness over the bridge of the nose.

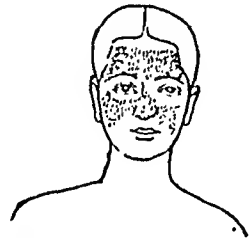


Fig. 9. Case 9.—Symptoms: numbness, formication, itching inside the ears and of the eyes.



Fig. 10. Case 10.—Symptoms: irresistible itchiness over forehead and eyebrows.

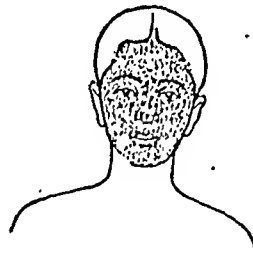


Fig. 11. Case 11.—Symptoms: burning sensation, numbness, loss of sensation over the face. Loss of pain sensation over areas marked with X.

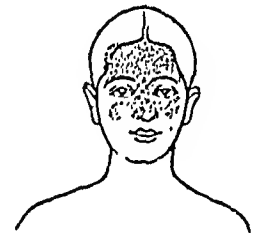


Fig. 11a. Case 11.—Symptoms less marked; area affected less in extent.

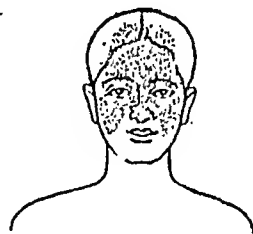


Fig. 12. Case 12.—Symptoms: itching and formication over face, forehead and inside the ears. Slight trophic (?) change noticed on the affected area.



Fig. 12a. Case 12.—Symptoms persisting over forehead and inside the ears, area affected distinctly less.

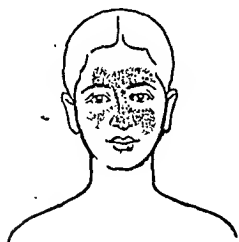


Fig. 13. Case 13.—Symptoms : heaviness, stiffness, formication. Twitching of some face muscles.

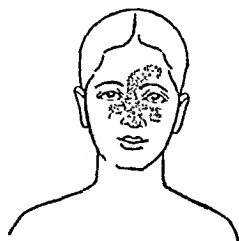


Fig. 13a. Case 13.—Symptoms less severe, area affected less in extent.

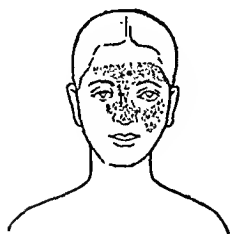


Fig. 14. Case 14.—Symptoms : numbness, loss of sensation, formication over cheek, forehead and inside the ears.

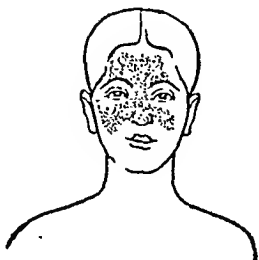


Fig. 15. Case 15.—Symptoms : itching and formication over forehead, face, inside the eyes and ears.

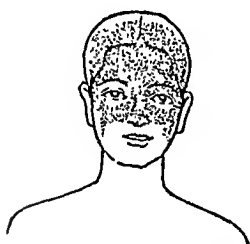


Fig. 16. Case 16.—Symptoms : distressing itching and formication over forehead and cheek, itching inside the ears and eyes.

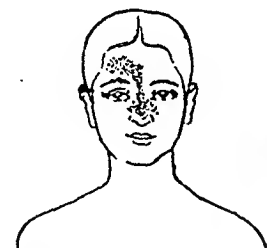


Fig. 17. Case 17.—Symptoms : sensory loss over forehead and face.

The dosage scheme of diamidino-stilbene was as follows :—

	Mean total dose (gm.) \pm s.d.	Mean relative dose (gm.) per 100 lb. body-weight \pm s.d.
Resistant cases ..	1.261 \pm 0.228	1.093 \pm 0.211
Ordinary cases ..	0.768 \pm 0.275	0.835 \pm 0.172

The number of injections was 12 in 2 and 15 in the rest of the resistant cases. Two ordinary cases had 9 injections each, 8 had 10 injections each and one case had 15 injections. In all these cases the dosage scheme described by Napier *et al.* was followed (Napier, Sen Gupta and Sen, 1942), and the maximum single dose

was 1 mg. per pound body-weight (about 2 mg. per kilo) in all cases. Only two of these 17 patients had severe reactions immediately after the injections; in others the reactions were not alarming.

Onset of symptoms of neuropathy

The symptoms appeared between 2½ and 5 months of the end of treatment; in 10 cases the symptoms appeared in 3 to 4 months. The onset of symptoms was insidious and apparently not accompanied with any other abnormality.

Subjective symptoms

The principal subjective symptoms complained of were : (a) disturbance of sensation, i.e. abnormal spontaneous sensations or paræsthesiæ, and (b) impairment of sensation, i.e. anæsthesia. In one case (case 1) hyperæsthesia to temperature and touch was also complained of. The paræsthetic symptoms complained of were numbness, heaviness, formication and itching.

The symptoms were limited to the forehead and face in all the cases, in one (case 5) there was extension to the neck. One patient complained of his face muscles twitching as if he had electric shocks. Some of the patients (cases 9, 12, 14, 15 and 17) complained of itching inside the ears and of the eyes, and there was no local cause to explain these symptoms.

The symptoms were very troublesome in some cases, and led to uncontrollable scratching and rubbing over the area affected. This apparently caused pigmentation and rubbing off of eye brows in a few cases (cases 4, 5, 12 and 16). In others the symptoms were much less troublesome, but made the patient feel rather uncomfortable.

Twitching of muscles, particularly, of the orbicularis oculi giving rise to a constant 'blinking' movement of the eyelids, was seen in three cases (cases 2, 4 and 5). Two patients complained of twitching of some of the face muscles.

Physical signs

On neurological examination the characteristic abnormality noted in all these cases was a peculiar dissociated anæsthesia over variable parts of the area supplied by the sensory branches of the trigeminal nerve. There was loss of sensation of light touch, with the preservation of sensation of pain, temperature and pressure. In one case the area affected extended to the neck over the area supplied from the second, third and fourth cervical spinal segments. In three cases the sensation of pain was also affected in small parts of the areas affected by dissociated anæsthesia. In two cases this anæsthesia was found over the lateral aspect of the concha of the ears.

Slight trophic changes were discernible in four of the cases (cases 4, 5, 12 and 16). The skin appeared to be more rough and dry, with increase of pigmentation, the eyebrows were

TABLE

Case number	Race, sex and age	Type of case	Di-amidino-stilbene a b c	Immediate reaction to injection	Onset of symptoms in months after treatment	Symptoms and signs	Period of observation in months	Progress
1	Ind. M. 34	O.	15 1.535 1.298	Mild	3	See fig. 1	..	
2	E. M. 40	R.	15 1.66 0.934	Mild	3 to 4	See fig. 2	16	See fig. 2a.
3	A.-I. M. 26	R.	15 1.36 1.225	Mild	4	See fig. 3	22	See fig. 3a.
4	E. M. 15	O.	10 0.96 0.784	Mild	3	See fig. 4	12	See fig. 4a.
5	A.-I. F. 37	R.	12 1.05 1.034	Mild	3	See fig. 5	18	See figs. 5a and 5b.
6	Ind. M. 25	O.	10 0.575 0.674	Moderate	3½	See fig. 6	12	Almost unchanged.
7	Ind. M. 40	R.	15 1.23 1.434	..	3½	See fig. 7	..	
8	Ind. M. 35	R.	15 1.25 1.101	Severe	5(?)	See fig. 8	22	Area affected unchanged, symptoms less severe.
9	Ind. M. 25	O.	10 0.815 0.802	Mild	2½	See fig. 9	13	Symptoms less severe, area affected unchanged.
10	Ind. F. 15	O.	10 0.695 0.911	..	3	See fig. 10	..	
11	Ind. M. 25	O.	9 0.69 0.78	..	3	See fig. 11	9	See fig. 11a.
12	Ind. M. 17	O.	10 0.665 0.743	Mild	3 to 4	See fig. 12	21	See fig. 12a.
13	Ind. M. 41	R.	12 1.015 0.830	Mild	7	See fig. 13	10	See fig. 13a.
14	Ind. M. 23	O.	10 0.635 0.917	Mild	3	See fig. 14	10	Symptoms less severe, area affected unchanged.
15	Ind. F. 41	O.	10 0.625 0.803	Severe	4	See fig. 15	..	
16	Ind. M. 15	O.	9 0.635 0.652	Mild	4 to 5	See fig. 16	12	Extent of area affected, unaltered; symptoms distinctly less.
17	Ind. M. 20	O.	10 0.625 0.822	Mild	2½	See fig. 17	..	

Ind. = Indian.
E. = European.
A.-I. = Anglo-Indian.

M. = Male.
F. = Female.
R. = 'Resistant' case.
c = Relative dose (g.) per 100 lb. body-weight.

O. = Ordinary case.
a = Number of injections.
b = Total dose (g.).

stunted in growth, and the hair over the affected area of the scalp (in one case) appeared less dark than over the rest of the head. It is difficult to say whether these changes were caused by the neuropathy or were the result of constant rubbing and scratching over the areas; probably the latter was the cause.

No other neurological abnormality was detected in any of these cases. All patients except two were cured of kala-azar. The two patients who had relapse of kala-azar were subsequently cured (of kala-azar) with other drugs.

Discussion

There can be no doubt that the neurological lesion was caused by a delayed toxic action of diamidino-stilbene. Similar symptoms have been entirely absent in Indian kala-azar untreated or treated with the different antimonials. The appearance of the symptoms at a more or less constant period (3 to 4 months in most cases) after the cessation of treatment with this drug, the absence of any other cause likely to produce the symptoms, and the fact that the syndrome is unlike that of any recognized diseases of the nervous system also point to the drug being the toxic agent responsible for the causation of this syndrome.

Incidence.—This condition has been encountered in 17 out of 104 cases of kala-azar treated with this drug at the hospital of the School of Tropical Medicine. The incidence of this condition is thus about 16 per cent.* We must however bear in mind the fact that it has not been possible to follow all cases treated, and that probably only the more intelligent and sensitive cases came under observation. It is quite possible that cases having slight degrees of the affection have not reported to us, the symptoms being very mild.

The incidence of this sequel seems to be higher in the 'resistant' cases than among the ordinary cases; there were 6 cases in 26 'resistant' cases treated, and 11 cases out of 78 ordinary cases. The difference is however not statistically significant.

Relation to dosage.—It is not possible to say whether the dosage employed in the cases of kala-azar was responsible for causing the neuropathy, because the same dosage scheme was applied to the whole series of cases, and the neuropathy occurred in about one-sixth of them. Moreover, the mean and standard deviations of the relative dosage per 100 lb. body-weight were not significantly higher in these cases than in the whole group of cases, though the total dose was relatively larger. (For dosage scheme

employed in the treatment of kala-azar with diamidino-stilbene, see Napier *et al.*, 1942.)

Relation to (immediate) reactions to injections.—The degree of immediate reaction to the injections of diamidino-stilbene was no measure of the tendency of the patient to develop neuropathy. Most of the 17 patients had mild reaction after the injections, there was moderate to severe reaction in three cases only. One of the patients (case 8) who had a severe reaction after the injection of diamidino-stilbene developed what may be called a minimal degree of lesion. Of the cases of kala-azar treated with diamidino-stilbene, 25 patients had what may be called moderate to severe reaction and the rest had a mild or no reaction; 3 out of 25 cases who had severe reaction developed neuropathy and 14 out of 79 who had a mild or no reaction. The difference is not significant.

The site and the nature of the neurological lesion

From the analysis of the symptoms it will be evident that the salient features are: (i) subjective sensory disturbances, paræsthesia and anæsthesia over parts of the area supplied by the trigeminal nerve; (ii) dissociated anæsthesia, loss of sensation of light touch with preservation of sense of pressure, pain and temperature, over variable parts of the trigeminal area; and (iii) the absence of nerve lesions elsewhere.

We have now to discuss the site of neurological lesion and its probable nature.

The fact that there were persistent objective sensory disturbances over the affected area rules out the possibility of trigeminal neuralgia.

It is unlikely that the lesion is of the nature of peripheral neuritis because the distribution of the objective signs in most cases did not correspond to the whole of the distribution of any one of the branches of the fifth nerve, because there was no tenderness of the nerves in any case, and because there was persistent dissociated anæsthesia of a particular type. Interstitial neuritis affecting the branches of the fifth nerve often causes pain referred to along the cutaneous areas of their distribution, and there is cutaneous anæsthesia and analgesia. These features were absent in these cases.

In neural leprosy some degree of dissociated anæsthesia is seen in many cases but rarely confined to the fifth nerve distribution, the anæsthesia often becomes complete later, and other signs of leprosy become evident (Lowe, personal communication, 1943). In the cases under consideration, the dissociated anæsthesia remained almost unchanged during the whole period of observation, and the features pointing to involvement of peripheral nerves were entirely absent.

It is believed that the Meissner's corpuscles are probably concerned in the appreciation of light touch. The type of dissociated anæsthesia seen in these cases might be caused by selective damage by the drug of the Meissner's corpuscles,

* Note regarding the incidence of the neuropathy by Dr. C. Chandra Sekar, Assistant Professor of Vital Statistics and Epidemiology, All-India Institute of Hygiene and Public Health: 'Using a 95 per cent confidence limit, it is estimated that the true chance lies between 0.10 and 0.25, i.e. if a very large number of individuals were taken, the percentage will not exceed 25 nor fall below 10'.

MENTAL SYMPTOMS IN PELLAGRA AND NICOTINIC ACID DEFICIENCY

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MENTAL symptoms have been regarded as one of the characteristic features of pellagra since 1735 when Gasper Cassal studied the first case and called it '*Mal de la Rose*'. The present name was given by an Italian physician, Francesco Frapolli, who published a careful account of the disease in 1771. Since then, cases of pellagra have been reported by workers all over the world.

The psychiatric importance of pellagra

The psychiatric importance of pellagra is considerable. It has been estimated that from 4 to 10 per cent of all pellagrins show mental symptoms (Henderson and Gillespie, 1940). In England, pellagra has been noted in lunatic asylums since 1913. There were 21 deaths from pellagra in 1922, mostly from the Lancashire

(Continued from previous page)

Summary

1. Seventeen of over one hundred cases of kala-azar treated with 4 : 4' diamidino-stilbene subsequently developed a neurological syndrome.

2. The principal features of this syndrome are paræsthesia and partial anæsthesia in the trigeminal area with loss of sensation of light touch, with preservation of sensation of pain, temperature and pressure.

3. The lesion is in the principal sensory nucleus of the trigeminal nerve in the pons, and is probably of the nature of a toxic degeneration. Diamidino-stilbene is the toxic factor responsible, and the selective toxic action is probably due to the ethylene component of this compound.

4. The condition is not dangerous to life and is not progressive; in most patients there is a tendency to slow recovery.

5. In cases having troublesome paræsthetic symptoms, all therapeutic measures (non-surgical) have been found to be useless except injections of solution of cobra venom (1 : 100,000) in gradually increasing doses which produces some degree of subjective improvement.

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Mental Hospital, Rainhill, and during the period 1913 to 1918 there have been 104 deaths from pellagra among the asylum inmates. Goldberger found that in certain asylums in the United States the number of lunatics developing pellagra each year was a constant proportion of the total (Manson-Bahr, 1940). Conditions are however quite different in the mental hospitals of this country. It is interesting to note that during the period 1936 to 1940 not a single case of pellagra has been reported from the Indian Mental Hospital, Kanke, which is the biggest mental hospital in this country and caters for the three provinces of Bihar, Bengal and Orissa (Dhunjibhoy, 1938, 1939, 1940, 1940a; Das, 1942). As early as 1915, Singer (Strecker and Ebaugh, 1935) realized the psychiatric importance of this disease and described it under three broad groups. His first group consisted of patients who developed mental symptoms, mostly depression and delirious states as a result of the disease itself. In the second group he placed those cases of manic depressive psychosis, dementia præcox and psychoneurosis in which pellagra had acted as a precipitating factor. His third group was formed of those patients who were already suffering from certain organic diseases of the brain, such as arteriosclerotic dementia, senile or presenile psychosis and general paralysis, patients in whom pellagra subsequently developed.

Miller and Ismail (1920) made an investigation into the incidence of the pellagra psychosis in Egypt and found that such cases formed 27.6 per cent of all admissions made into the Khanka Mental Hospital. They studied 757 cases. The cases were classified on admission into acute confusional psychosis; mania, acute, recurrent and febrile; melancholia, simple and recurrent; dementia, imbecility, adolescent insanity, epileptiform insanity and general paralysis of the insane.

Mental symptoms in pellagra reported in this country

Pellagrins showing mild depression, melancholia, mania, restlessness, irritability and clouding of the consciousness have been studied in this country by Lowe (1931), Raman (1933), Gupta (1935), Panja (1935), Dhyagude and Khadilkar (1939), Goodall (1940), Ahmed (1942, 1942a), Batra (1942), Patel and Shah (1942), Patel and Motashaw (1942), Heilig (1943), Napier and Chaudhuri (1943) and Dey (1943). Lowe (1931) studied 40 cases of pellagra occurring among the lepers at the Leprosy Hospital, Dichpali, Hyderabad, Deccan, and noticed marked mental symptoms in three of them. One showed marked melancholia with periods of mania and suicidal tendency. Another patient became semicomatose and had periodic attacks of epileptiform fits. A third case showed extreme depression verging on melancholia and finally committed suicide by

drowning. Lowe's patients who showed marked mental symptoms invariably died. Mody (1935) reported a typical case of pellagra with characteristic skin and gastro-intestinal manifestations. He was taciturn and morose and often suffered from hallucinations. His mental attitude was pessimistic as he believed that he would never get well. Treatment was however effective in removing the other manifestations of pellagra though the mental condition remained stationary. Raman (1940) reported two cases of pellagra with mental symptoms. In one of them, mental symptoms were so severe that the patient could be controlled only with hyocine injections. With treatment, the general condition of the patient improved but the mental condition did not show any amelioration. He had later on to be transferred to a mental hospital, where he subsequently died.

Mental symptoms in pellagra and their response to treatment

The prognosis of pellagra has considerably improved with the introduction of nicotinic acid therapy. Fouts *et al.* (1937) treated four cases of 'alcoholic pellagra' with relatively large doses of nicotinic acid and noticed improvement in their mental condition within 24 hours of the treatment. Smith *et al.* (1937) obtained good results with 50 mg. of nicotinic acid given daily over a period of 12 days, the patients showing improvement in their mental condition in about 48 hours. Spies *et al.* (1939) found dramatic improvement in treated patients showing acute mental symptoms. These symptoms, varying from slight confusion to delirium and mania, disappeared rapidly, often overnight. The maniacal patients became calm and the confused patients mentally clear. Apathy and lassitude gave way to interest. After therapy, they readjusted themselves and often had excellent memory of their actions, ideas and surroundings during the psychotic period. Patients suffering from irritability, abdominal pains, weakness and difficulty in walking improved considerably under the combined therapy of nicotinic acid and vitamin B₆ (Spies *et al.*, 1939a). Similar results have been obtained by Matthews (1938), Rachmilewitz and Glueck (1938), Bogart (1938), Goodall (1940), Ahmed (1942), Batra (1942), Patel and Shah (1942), Patel and Motashaw (1942) and Dey (1943). This is only one side of the picture as we often come across cases in which nicotinic acid does not cause any improvement in the mental condition of the patient.

The case described below is one of this nature.

Case 1.—A Hindu male, cultivator, aged 38 years, of Gaya district, came under the author's observation on the 14th May, 1942, with the following complaints: (1) diarrhoea for the last 5 months, and (2) weakness and inability to do any work for the last 2 months.

The patient is the third child of healthy parents. There is no history of mental illness in the family. He was married at the age of 18 years and has three healthy children.

His diet consisted of rice, pulse, vegetables and milk. He is not addicted to any intoxicant and is an orthodox Brahmin.

He has not had good health from 1935 or 1936. His main troubles have been occasional attacks of diarrhoea, dysentery, constipation and flatulence. Since then he has been constantly losing weight. He was robust and healthy before, but is now emaciated.

He was a happy, care-free man. He loved his children and took an interest in his work. He had many friends in his village. His uncle noticed a change in his character in 1939. He became irritable and quarrelsome. He began to avoid the company of his friends. His children were afraid of him as he beat them on the slightest pretext. He did not take care of his property and always accused him (his uncle) of misappropriation. His attitude to his wife also changed.

The patient was pale, thin and emaciated. His weight was 98 lb. and height 5 feet 6 inches. There were symmetrical patches of scaly dermatitis with marked pigmentation, sharply demarcated from the surrounding skin on the dorsum of the feet and front of the legs.

His tongue was flabby with indentations on the margin. The abdomen was tumid and tympanitic, with gurgling in the iliac fossæ. He was passing five to six loose motions daily. Repeated examination of the stool revealed no abnormality. Neurological examinations revealed nothing.

Mental examination: He was found sitting in a sad and apathetic mood. He took no interest in his surroundings. He dressed carelessly and was often found lying naked in his bed. He passed faeces and urine in the bed, and did not have the bed cleaned. His facial expression was vacant; saliva was dribbling from his mouth. When he ate, he did not wash his mouth but left it till some one cleaned it for him. He did not relish food but took it when it was given. He was always absent-minded and depressed. Questions had to be repeated several times before a response could be elicited from him. Speech was slow and coherent but rarely spontaneous. Memory for both recent and remote events was impaired. Orientation in time was impaired. Orientation in place and person was good. His judgment was poor. He had insight into his illness.

He was put on the following treatment: (1) nicotinic acid 50 mg. tablets, 2 tablets, three times a day, (2) liver extract, 2 c.cm. intramuscularly on alternate days, and (3) fersolate tablets, one tablet, three times a day after meals. His diarrhoea disappeared on the third day of this treatment and his skin condition completely cleared up in a fortnight. The mental condition of the patient, however, showed no improvement, though he took the drug for about 2 months.

Mental symptoms in nicotinic acid deficiency

Recently, American authors have drawn attention to the occurrence of neurotic and neurasthenic manifestations in sub-clinical states of vitamin deficiency (Jolliffe, 1941; Ruffin, 1941). Spies *et al.* (1938) studied 60 patients with mental symptoms but without the characteristic skin and gastro-intestinal manifestations of pellagra. Their patients showed loss of memory, delirium, mania, depression, and many of them presented symptoms of a neurasthenic nature, viz, fatigue, insomnia, anorexia, vertigo, palpitation, headache, nervousness, unrest, apprehension, anxiety, forgetfulness and paræsthesia. Some of them showed paranoic reactions with fears of relatives and delusions of persecution. Treatment with nicotinic acid led to recovery in all cases within 6 days. Sydenstricker and Cleckley (1941) studied 29 such patients with symptoms of active psychosis but with no signs of pellagra.

They showed some of the following signs: manic excitement, delirium, hallucinations, disorientations and delirium tremens. It was possible to show that in 22 of them, symptoms were due to nicotinic acid deficiency while in others it was probably due to psycho-neurosis, arteriosclerosis, senility and other factors. Cleckley *et al.* (1939) found remarkable improvement with this drug in 19 stuporous patients, and Evans (1939) in a case showing schizophrenia-like psychoses. A similar case has been reported by Slater (1942) in England. His patients showed symptoms suggestive of a melancholic, a schizophrenic and an organic state. This case made dramatic recovery with nicotinic acid.

Two such cases came under the author's observation recently:—

Case 2.—A Hindu male, aged 18 years, of Monghyr district, came under the author's observation on the 28th February, 1942, with the following complaints: (1) restlessness, getting worse every day for the last 10 days, (2) insomnia for the last 5 days, and (3) diarrhoea for the last 10 days.

He was the second of four children of over-indulgent parents. Both the parents were healthy and so were the other children. There was no history of psychosis in the family. The patient was a man of temperate habits and was not addicted to alcohol, toddy or any other intoxicant. He was considered to be social and well behaved. He took part in sports. He was an average boy in school. He was unmarried. His diet consisted of rice, pulse, and ordinary vegetables. He occasionally took meat. He had typhoid at the age of 10 and dysentery at 12.

About 6 months ago, the patient received the news of his failure at the supplementary matriculation examination. This gave him a shock, but he was not broken-hearted, and started his studies in earnest. It is said that he read for about 6 to 8 hours at night in addition to his studies during the day. During this period, he paid little attention to his food and often went without it at night. Even when he was not at work, he remained alone and took no interest in his family or friends. He gave up sports. During this period, he would frequently have loose motions, several times a day, and would then often pass 2 or 3 days without any. He continued in this way for about 3 months. Then he started getting headache which was very annoying as it disturbed his studies. Often he was seen tossing in bed and on enquiry he would say that he had a mild attack of headache. His father advised him to stop his studies for the time being, and start again after he was well. He paid no attention to his father's advice, and his father says that he was getting more irritable every day. Twice during the last 3 months he had colicky pains in his abdomen but he refused treatment. He was having loose motions, 5 to 6 times a day for the last 10 days, which was attended with griping. He could not sleep for the last 5 days and was very restless. He often spoke at random for 2 to 3 hours at a time. He often made attempts to run away from the house and was calm and quiet at times.

Mental examination revealed flight of ideas, elation and a sense of grandeur. He appeared also to be suffering from hallucinations and delusions of persecution but refused to say anything about them. He refused to answer questions and believed that every one was either a fool or his enemy. At times he was violent, particularly on the night he was seen by the author. He was making attempts to leave the bed, and 5 persons found it difficult to keep him under control. Orientation in place, person and time was good. Memory could not be tested.

The patient was lean, thin and emaciated. His height was 5 feet 5 inches and weight 100 lb. His tongue was pale and flabby. His abdomen was distended and tympanitic. There was no obvious skin disease. Examination of the central nervous system revealed no abnormality. Repeated examination of the stool showed nothing.

The patient was treated with hydrotherapy and sedatives combined with nicotinic acid, 50 mg. tablets, 2 tablets three times a day. The presence of vague abdominal symptoms suggested nicotinic acid deficiency, and nicotinic acid was given in the hope that it would ameliorate abdominal symptoms. Curiously enough the patient recovered completely on the third day of the treatment. He had good sleep on the second night and was perfectly sane on the third day.

Case 3.—A Hindu boy, aged 8 years, of Patna district was bitten by a street dog on the 13th March, 1943. He came for treatment to the out-patient department of the Pasteur Institute, Medical College Hospital, Patna, 2 days later. He is the only child of his parents, who were healthy. There is no history of mental illness in the family. Treatment was started on 15th March, 1943, and he was given seven injections of anti-rabic vaccine. He got an attack of delirium at 4 p.m. on 21st March, 1943. He became very apprehensive and restless. He cried at the top of his voice but gave no reasons for it. He tried to throttle himself and was prevented from doing so. His father poured a bucketful of water over his head but to no effect. He became quiet in about an hour and went to sleep. His sleep was disturbed. Next day when an enquiry was made about his fear and cry, he said that a little before the attack he felt that something like air had entered his neck and was throttling him. He saw monkeys and dogs coming to attack him. No vaccine was given on 22nd March, 1943 and 23rd March, 1943, as the anti-rabic treatment was suspected to be responsible for it. The attacks of delirium, however, recurred again on 22nd March, 1943 and 23rd March, 1943, at the same time. Vaccine was restarted and the patient was given nicotinic acid, 50 mg. tablets, one tablet three times a day. There was no further attack and the patient was given a full course of 14 injections.

Comments

The first case is a typical case of pellagra with gastro-intestinal, dermal and mental manifestations characteristic of the disease. It is interesting to note that while the gastro-intestinal and dermal lesions disappeared readily with nicotinic acid, mental symptoms remained stationary. The patient developed mental symptoms in the course of the disease. He had already suffered from vague abdominal disturbances for 3 years before his uncle noticed a change in his character. The mental symptoms were probably a manifestation of pellagra. Cases of this nature, where mental symptoms have proved resistant to treatment, have already been reported by Mody (1935), Jersild (1941) and Petri *et al.* (1937). In the present state of our knowledge it is difficult to give any definite explanation. The possibility of certain organic changes having taken place in the brain, incapable of repair on supplying the deficiency, should not be lost sight of, and post-mortem evidence of this nature have been found by Dunlap and Watson (Henderson and Gillespie, 1940). On the other hand Bogart (1938) has reported a case of dementia which was promptly cured by nicotinic acid.

The mental condition of the patient formed the prominent feature of the last two cases. The

second case was seen in a maniacal condition and had no skin lesions. The third case was in a delirious state, and both the skin and gastrointestinal manifestations were conspicuous by their absence. Both of them made a dramatic response to nicotinic acid and thus appeared to be cases of nicotinic acid deficiency. Cases of this nature have already been studied by Spies *et al.* (1938), Cleckley *et al.* (1939), Sydenstricker and Cleckley (1941), Jolliffe (1941) and Ruffin (1941) in America and Slater (1942) in England. No such case appears to have been reported so far in this country. Cases of nicotinic acid deficiency are quite common here, and it is likely that many more cases of this nature may come to light if a note is made of their existence.

Conclusions

Mental symptoms in pellagra are legion, and we find that pellagra can simulate any one of the psychoses or psycho-neuroses met with in practice. At present it is difficult to associate any one in mental state with this syndrome, but depression is the usual effect seen in such patients. Mental symptoms without any other signs of pellagra occur in cases of nicotinic acid deficiency and show dramatic improvement when the deficiency is supplied.

Summary

1. A review of the recent articles on the subject has been given.

2. Attention has been drawn to the occurrence of only mental symptoms in cases of nicotinic acid deficiency, and two such cases have been reported.

3. One case of typical pellagra has been reported in which the mental symptoms proved resistant to nicotinic acid therapy.

Acknowledgments

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PRELIMINARY OBSERVATIONS ON THE USE OF *RAUWOLFIA SERPENTINA* BENTH. IN THE TREATMENT OF MENTAL DISORDERS

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Introduction

THE root of *Rauwolfia serpentina* Benth. has been used in the treatment of insanity in India for centuries. Sen and Bose (1931) and Chopra, Gupta and Mukherjee (1933) investigated the pharmacological action of the root extract and of the alkaloidal base respectively. Siddiqui and Siddiqui (1931) isolated several alkaloids from the root of the plant. The pharmacological actions of some of these alkaloids have been studied by Chopra and Chakravarti (1941) and also by Chopra *et al.* (1942). Ever since the publication of the results of these pharmacological investigations, the use of an alcoholic extract of the root of *Rauwolfia serpentina* for the treatment of hyperpiesis and of certain forms of insanity has increased considerably. *Rauwolfia serpentina* deserves a definite place in the pharmacopoeia of modern medicine. Side by side with the use of the alcoholic extract of the root, the use of the powdered root in the treatment of certain types of insanity by all classes of physicians—Ayurvedic, Unani and scientific—has greatly increased. We do not know the exact volume of the trade in the *Rauwolfia serpentina* products but, judging by the requests we receive for the standardized extract prepared by the School of Tropical Medicine, it must be considerable. But it is noticeable that very few clinical reports on the use of *Rauwolfia serpentina* have been published. We therefore publish the following observations on the use of the standardized extract.

Materials.—The patients were inmates of a mental institution suffering from various types of mental disorders. Initially the powdered root (20 to 60 grains once a day) was used, though this was a very efficient sedative, it produced a great depression of the respiration. In many patients the respiration became so shallow and infrequent that they developed cyanosis. It was therefore thought expedient to use the standardized extract in the present series of cases. The extract was used twice daily at noon and at 8-30 p.m. before meals unless otherwise stated: no other treatment was given. Respiration was not apparently depressed.

Case notes

Affective reaction type

(1) K. P., male, age 35, talks incoherently, is restless, eats voraciously, and does not sleep well. Diagnosis—

manic excitement. P/R—76/16; B.P.—120/80. Duration of symptoms is 4 months: previous treatment symptomatic, with sedative drugs ineffective.

Standardized extract of *Rauwolfia serpentina* $\frac{1}{2}$ drachm was given twice daily for 7 days. The patient became quiet and had 6 hours of continuous sleep beginning 2 hours after the last daily dose at 8-30 p.m. The patient was clinically much improved.

(2) N. S., male, age 20, cyclothymiac—becomes excited and unmanageable every summer for 2 to 3 months for the last 4 years: talks at random, is sexually excited and behaves obscenely. Diagnosis—depressive psychosis with manic excitement. P/R—80/18; B.P.—118/74. Previous treatment with sedative drugs—hypnotic effect only.

Extract *Rauwolfia serpentina* $\frac{1}{2}$ drachm was given twice daily. The patient responded well, became quiet, and could sleep for 6 to 7 hours at night.

(3) A. C., male, age 20, hyperactive, sleeps badly: duration 3 months. Diagnosis—hypomania. P/R—80/18; B.P.—118/70. Previous treatment with sedative drugs ineffective.

Extract *Rauwolfia serpentina* $\frac{1}{2}$ drachm was given once a day, ineffective; next day 1 drachm given once. Sleep was induced 3 hours after the dose and lasted for 8 hours. Patient clinically improved.

(4) P. C., male, age 30, cyclothymiac, repeated maniacal attacks. Duration of present attack—3 months, talks incoherently, flight of ideas present, overactive, restless. Diagnosis—acute mania. P/R—90/18; B.P. not taken, the patient unco-operative.

Extract *Rauwolfia serpentina* $\frac{1}{2}$ drachm was given twice daily, sleep was induced on the 3rd day after the beginning of the treatment and lasted for 5 hours. Patient much improved.

(5) S. M., male, age 40, an old inmate of the hospital, garrulous, overactive, elated, dresses fantastically, dirty in habits. Diagnosis—chronic mania.

Extract *Rauwolfia serpentina* $\frac{1}{2}$ drachm was given twice daily during a period of restlessness. The patient became quiet and slept for an average of 6 to 7 hours daily.

Schizophrenic type

(1) M. B., male, age 17, moody, reticent with loss of interest for a few days: at times impulsive in behaviour: sleepless. Diagnosis—schizophrenia. P/R—90/16; B.P.—108/70.

Extract *Rauwolfia serpentina* $\frac{1}{2}$ drachm was given twice daily, slept soundly for 6 hours at night and improved clinically.

(2) B. W., male, age 18: stereotypy in speech and movement, sudden fits of anger, sleeps badly. Diagnosis—schizophrenia. P/R—86/20; B.P.—104/68.

Extract *Rauwolfia serpentina* $\frac{1}{2}$ drachm was given twice daily on three occasions; each time he slept for 6 to 7 hours continuously at night.

(3) B. P., male, age 20, giggles, grimaces, talks to imaginary persons (hallucination). Diagnosis—chronic schizophrenia. P/R—80/16; B.P. not taken.

Extract *Rauwolfia serpentina* $\frac{1}{2}$ drachm was given twice daily, became quieter and slept for 5 to 6 hours at night.

(4) S. B., male, age 22, a good student: ambition for higher studies in England not fulfilled: became irritable, attacked his father: mental agitation, insomnia. Diagnosis—schizophrenia. P/R—80/18; B.P.—110/76.

Extract *Rauwolfia serpentina* $\frac{1}{2}$ drachm was given twice daily—the patient cooled down and slept for about 8 hours per night—much improved.

(5) M. B., male, age 24, an inmate of the hospital for more than a year: mute, impulsive, sleepless, attacks people, dirty in habits, remains nude. Diagnosis—chronic schizophrenia with dementia. P/R and B.P. could not be taken.

Extract *Rauwolfia serpentina* $\frac{1}{2}$ drachm was given twice daily. Sleeps for 8 hours on an average after the extract was given.

(6) A. G., male, age 26, refuses to take food, mutters to himself—no sleep at all. Shows marked negativism.

Diagnosis—acute schizophrenia. P/R and B.P. not taken.

Extract *Rauwolfia serpentina* 1 drachm once a day. The patient slept for about 6 hours a day after the drug.

(7) N. B., male, age 39; auditory and visual hallucinations and bizarre delusions of persecution and sin. Diagnosis—paraphrenia. P/R—80/18; B.P.—116/86.

Extract *Rauwolfia serpentina* $\frac{1}{2}$ drachm twice daily. Slept continuously for 6 to 7 hours at night.

Organic reaction type

(1) M. H., male, age 30, ganja (*Canabis indica* resin) smoker, emotionally unstable, verbose, disoriented about time and space—a poor sleeper. Diagnosis—confusional insanity. P/R—100/20; B.P.—106/72.

Extract *Rauwolfia serpentina* $\frac{1}{2}$ drachm was given twice daily. The patient slept for 5 to 6 hours on an average after the drug was used.

(2) S. S., male, age 55, an inmate of the hospital for several years, mental disorder traceable to a head injury in childhood—intellectual capacity impaired after the accident. Developed manic excitement years ago. An opium addict, shouts loudly, speech indistinct, moves his arm while talking. Sleepless during periods of excitement. Diagnosis—amentia with manic excitement and opium addiction. P/R—70/16; B.P.—120/76.

During a period of excitement—the extract $\frac{1}{2}$ drachm was given twice for one day only. The patient fell asleep 2 hours after the last dose and slept for 6 hours, and on awakening he remained quiet and the period of excitement was cut short.

Epilepsy

S. M., male, age 21, history of trauma at birth (forceps delivery); had fits after birth for 3 or 4 days. Later epilepsy developed, fits occurred every 3 or 4 months; now gets fits every 10 to 12 days. Major fits—3 to 4 a day—last for 5 minutes. Minor fits alternate with major ones. History of status epilepticus; aura, tingling sensation moving up the right arm; post epileptic automatism present; the patient is blind on account of untreated glaucoma following epidemic dropsy at the age of 15. Left handed; speech indistinct, reflexes less intense on the right side. Intelligence retarded, impulsive, suggestible, religiously minded; memory not impaired. Fits increase after meat diet. P/R—64/16; B.P.—110/80.

Treatment: Diet strictly vegetarian.

Extract *Rauwolfia serpentina* 15 minims twice daily started 10 days after a major fit, i.e. when a major fit was expected. Pulse and blood pressure as also the hours of sleep in 24 hours were noted.

Sleep—duration 11 hours in 24 hours.

Pulse came down to 54, B.P. 80/56 on the 5th day necessitating withdrawal of the drug for 2 days—B.P. 98/60, and a minor fit occurred. The extract was repeated in small doses (2 to 4 minims) once at bed time. Major fits were stopped but minor fits continued to occur at longer (2 to 3 days) intervals. With the control of major fits the patient showed great clinical improvement. This patient was treated at his home.

Discussion

Sedatives and hypnotics occupy a very important place in the treatment of psychopathics. In fact, in spite of the great advance in the psychological treatment—psychoanalysis, hypnosis, suggestion and other methods of psychotherapy—and the great improvement of the general measures available for the rational management of mentally diseased persons and the introduction of newer methods of treatment, the production of shock following convulsions

induced by insulin, cardiazol or by the inductotherm, organotherapy, hydrotherapy and occupational treatment, in spite of all these factors sedatives and hypnotics are still indispensable. Many of these psychopathic persons are agitated and excited, usually obviously so; but sometimes their inner mental agitation may be masked by a complete isolation from the world of realities. Because of this inner stress, the physiological mechanism of sleep is disturbed, and restful sleep is extremely rare in these persons. Continuous bodily and mental agitation and insomnia prevent recuperation of body and mind, and cure is delayed. Apart from this, continuous sedation, in some forms of mental disorder at least, depresses the mechanism which started the disorder and thus may act almost as a specific. Various sedatives and hypnotics have been used but the ideal sedative has not yet been found. A drug easily administrable, sure, without any other undesirable side action and with a prolonged sedative action is the drug of choice. The principle responsible for the sedative effect in the *Rauwolfia serpentina* root has not yet been identified beyond doubt. Gupta and Kahali found that, in experimental animals, even though the purified total alkaloidal base shows little sedative action, the alcoholic extract of the root is not only sedative but also hypnotic. In the cases reported here, *Rauwolfia serpentina* never failed to induce sedation and sleep, and the patients showed undoubted clinical improvement after its use. The extract of *Rauwolfia serpentina* also stimulates peristalsis of the alimentary tract. This is a desirable side action, as in most of the psychopathic patients there is a retardation of alimentary function. This action of the extract may be responsible for the improvement of appetite that was often noticeable in these patients.

Unfortunately the extract is a circulatory and a respiratory depressant. With a properly controlled dose of the standardized preparation, respiratory depression need not follow, but there is always a fall of blood pressure following the use of the extract. This side action may be desirable in the senile and arteriosclerotic patients suffering both from hypertension and mental disorder (excitement and insomnia) but in the majority of the psychopathic cases the blood pressure is more often normal rather than raised. The extract should be used with caution. A careful examination of the circulatory system, kidney and lungs should be made. The initial dose should be small and varied according to the weight and general physical condition of the patient. Pulse and blood pressure should be daily noted for proper control of the dose, which may be cautiously increased, if the circulatory condition permits, until the desirable limit of sedation is obtained. In experimental animals we have found that the extract has a prolonged action. The drug seems to be

(Concluded on opposite page)

SULPHAPYRIDINE ANURIA

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AGRANULOCYTOSIS and anuria are the two most important complications which may occur in

(Continued from previous page)

cumulative in action. This point should be borne in mind in spacing the doses.

Until more is known about the nature, site and mode of action of the sedative principle, it is not possible to state exactly how the drug acts in the treatment of psychopathies.

Conclusion

(1) Fifteen patients suffering from various types of mental disorder have been treated with the standardized extract of *Rauwolfia serpentina* Benth. Of these five suffered from disorder of the affective reaction type, seven from schizophrenia, two from organic psychoses and the remaining one from chronic epilepsy.

(2) All of these patients suffered from insomnia and showed considerable motor and mental agitation. The epileptic patient had frequent major and minor fits.

(3) The extract was given twice daily—at noon and at bed time usually in 30 minim doses. As the extract has a depressant action on the circulation, it is advisable to start with a smaller dose, e.g. minims 15 in well-nourished persons; under-nourished run-down patients should be given a smaller dose. The extract has cumulative action; the pulse and blood pressure should be carefully observed, and the doses accordingly controlled.

(4) Sleep ensued 2 to 3 hours after the evening dose, and lasted for more than 6 hours.

(5) The patients became quiet and behaved more normally, and those suffering from affective disorders showed considerable improvement.

(6) In the epileptic the major fits were stopped and the minor fits were controlled, with great clinical improvement.

(7) The alimentary functions of the patients were stimulated and appetite improved.

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treatment with sulphapyridine, and there are numerous references to them in medical literature. While the onset of agranulocytosis can generally be anticipated by white blood cell counts, the onset of anuria is often dramatic in its suddenness and severity.

This report records five cases of hæmaturia followed by anuria which occurred in patients undergoing sulphapyridine therapy for gonorrhœa. In one of the five the anuria was relieved by the giving of intravenous saline alone, but in the remaining four, cystoscopy with ureteric catheterization was performed, and rapid recovery followed in all cases.

In view of the extensive use of sulphonamide drugs for so many infective conditions, it is considered that attention should be drawn to the possibility of the occurrence of renal complications, to the means of preventing their onset, and to a satisfactory line of treatment.

Case 1.—Pte. H., age 24 years. Gonorrhœa (fresh). Dosage of sulphapyridine—22 grammes in 40 hours.

Symptoms.—Sudden onset of bilateral renal colic with vomiting. Patient passed 1 oz. of blood-stained urine immediately after the onset of the pain, and no urine in the subsequent five hours.

Treatment.—The left ureter was catheterized and blood-stained debris was washed out. There was a concretion at the lower end of the right ureter, and though this was broken up, the right ureter could not be catheterized. Intravenous drip saline for 24 hours. Complete recovery.

Intravenous pyelography a month later showed normal renal tracts and normally functioning kidneys on both sides.

Case 2.—Pte L., age 21 years. Gonorrhœa (fresh). Dosage of sulphapyridine—22 grammes in 40 hours.

Symptoms.—Sudden onset of epigastric pain which spread to both loins. Vomited any fluids which were given. Passed very small quantities of blood-stained urine.

Treatment.—Intravenous saline 1 pint (drip method). Passed 18 ounces of blood-stained urine, and thereafter the urine became normal. Complete recovery.

Case 3.—Pte. K., age 31 years. Gonorrhœa (fresh). Dosage of sulphapyridine—25 grammes in 4 days.

Symptoms.—Complained of suprapubic abdominal pain, and vomited. Passed one ounce of blood-stained urine at the onset of the pain and thereafter nil.

Treatment.—Intravenous drip saline caused no secretion of urine. On cystoscopy, crystal deposits were seen at both ureteric orifices which were swollen and œdematous. Catheters were passed up both ureters with difficulty, and debris was washed from them both. Complete recovery.

Case 4.—Pte. P., age 22 years. Gonorrhœa (fresh). Dosage of sulphapyridine—41 grammes in 7 days.

Symptoms.—Generalized intense morbilliform rash, nausea, fever, and hæmaturia. No abdominal pain, and no vomiting. Anuria for 12 hours, and became puffy under the eyes.

Treatment.—On cystoscopy it was seen that there were impacted deposits at both ureteric orifices. The left ureter was catheterized and washed out, but the intense œdema and swelling round the right ureteric orifice prevented this side being catheterized. Complete recovery.

Intravenous pyelography a month later showed normally functioning kidneys on both sides.

Case 5.—Pte. C., age 27 years. Gonorrhœa (relapse). Dosage of sulphapyridine—26 grammes in 3 days.

Symptoms.—Sudden onset of bilateral renal colic with passage of a small quantity of blood-stained urine. Anuria during the subsequent 6 hours. Vomited any fluids given.

Treatment.—One pint of intravenous drip saline had no effect. On cystoscopy greyish concretions were seen projecting from both ureteric orifices. These were broken up by ureteric catheters and both ureters were catheterized and washed out. Complete recovery.

Discussion

The urinary complications of sulphapyridine treatment are due to the insolubility in water of its excreted products, mainly acetylsulphapyridine, which forms crystals in the urinary tract. The appearance of these is characteristic—thin, sharp-pointed, and arranged in bundles like sheaves of corn. Hæmaturia is caused by the mechanical action of the crystals, and anuria by ureteric obstruction due to calculus formation and reactionary inflammation. This finding has been recorded in a fatal case in which death, confirmed at autopsy, was due to blockage of the ureters with crystals of acetylsulphapyridine (Carson and Smith, 1942). There is no evidence that blockage of the renal tubules is a factor in producing anuria.

On this assumption the rational line of treatment is to remove the ureteric obstruction, and this can be done by ureteric catheterization through a cystoscope. The procedure in the cases described involved the breaking up of concretions impacted at the ureteric orifices and catheterization with lavage of the ureters. Removal of the concretions presented little difficulty as they were soft, and were easily broken up by the point of a ureteric catheter, but œdema prevented catheterization of one ureter in two cases. Intravenous pyelography at a later date, however, showed normal excretion from both kidneys in these two cases. Difficulty comes from the fact that visibility in the bladder is poor owing to the cloud of debris, pus from the urethra, and blood.

In one case the administration of intravenous saline produced diuresis sufficient to remove the obstruction, and this treatment alone may be successful in a mild case without anuria. It should nevertheless be employed in all cases as a preliminary to other measures; most of the cases had vomited, and all were suffering from varying degrees of dehydration.

Rogan and Cruickshank (1942) have described a case of sulphapyridine anuria which was successfully treated by 'Inductotherm' applied to the loins; however they agree that this treatment would have no effect if obstruction were in the ureters.

It will be observed that the dosage of sulphapyridine varies considerably in the series. This is accounted for by the fact that the intensive method of treatment adopted a short time before cases 1 and 2 were treated was later stopped, and as a routine the usual seven-day course of one gramme sulphapyridine four-hourly was substituted. Previously a series of 200 cases of gonorrhœa (fresh) had been treated by this course of smaller dosage and no complications

had been observed. It appears that the risk of complications is greater with the intensive method of therapy, and notwithstanding the excellent results obtained by it, we do not consider that this justifies the risk.

As regards prevention, all cases were being given large amounts of fluids, and we emphasize, particularly in the tropics, the extreme importance of a large fluid intake for all cases being treated with sulphapyridine. Four of the five cases were on alkaline mixtures four times daily, but it is doubtful if, by the oral administration of drugs, the urine can ever be made sufficiently alkaline to affect the solubility of acetylsulphapyridine.

It is interesting to note that although there was a urethral discharge present in three of the cases when renal symptoms developed, instrumentation did not aggravate urethritis in any, and a complete cure of gonorrhœa has resulted in all.

We wish to thank Lieut.-Colonel J. W. Eames, R.A.M.C., for permission to publish these cases, and Captain W. J. Crisp, R.A.M.C., who was responsible for the surgical treatment of two of them.

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A Mirror of Hospital Practice

MONGOOSE BITE AND HYDROPHOBIA

By MOHD MOHSIN ALI ABBASI, M.B., B.S., P.C.M.S.

Assistant Surgeon, Samrala

A YOUNG Muslim male, aged 35 years, was bitten by a wild mongoose; the mongoose bit him on the right ear on or about the 4th June, 1943. He remained well and continued his work as an agriculturist, till 31st July, 1943, when he suddenly became ill.

On examination he complained of pain at the site of the scar, for two days, and inability to drink for the last few hours. His temperature was 100.6°F., he had a look of anxiety and was very restless.

On being given water to take, he exhibited the typical hydrophobic convulsive jerks and projected the water from his mouth. No salivation was present. Next day his condition worsened, he was thirsty and had air hunger, the whole body was drenched with perspiration. No fluids had been taken; the mind was clear but extremely anxious. Salivation was considerable. He died a few hours later.

The same mongoose is said to have bitten a cow on the same date on the nose and the cow is said to have died of hydrophobia 12 days before the man falling ill.

No case of rabies caused by a mongoose bite has as far as I know previously been reported.

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Indian Medical Gazette

NOVEMBER

AUTO-HÆMAGGLUTINATION

VISIBLE clumping of human blood corpuscles by human blood serum can be produced in three different ways :—

1. By true iso-agglutinins. These agglutinins are specific for their respective agglutinogens and this fact is the basis of blood-grouping tests.

2. By pseudo-agglutination, a marked form of rouleau formation.

3. By auto-hæmagglutinins or cold agglutinins. These are non-specific, act only below body temperature, and act on all human red-cells irrespective of their agglutinin make-up. Such agglutinins are not uncommonly found, but they are usually in such low titre and act only at such low temperatures that for practical purposes they can usually be ignored.

Sometimes, usually in pathological conditions, their titre rises markedly and they become active at room temperature even in the tropics. This is apparently the basis of the auto-hæmagglutination which we are now discussing.

This phenomenon of auto-hæmagglutination was defined by Boxwell and Bigger in 1931 as follows : 'Auto-hæmagglutination is a clumping of erythrocytes into irregular masses, visible to the naked eye, occurring in the presence of the individual's own serum, without bacterial action, at air temperature, and reversible at body temperature.' The phenomenon is usually observed by accident, in attempts to make blood counts or prepare thick blood films. Until recently this phenomenon has been regarded as a rare one, and in temperate countries it probably is rare. It is very rarely if ever found in normal persons, but it does appear occasionally in disease conditions particularly those associated with anæmia and/or jaundice. Moreover as long ago as 1898 it was pointed out by Kanthack and others that it was very common in trypanosomiasis (it was even suggested as a diagnostic test for this disease according to Manson-Bahr, 1924), and it has since been reported as occurring in a large variety of conditions but quite commonly in certain parasitic and protozoal diseases particularly in the tropics.

Numerous papers on the subject are scattered throughout the literature of the last fifty years,

and the older literature was well reviewed by Cohen and Jones in 1924 and by Boxwell and Bigger in 1931. The article of Cohen and Jones is reprinted in this issue, and Boxwell and Bigger have provided some of the material used in the present discussion. There are however several references since these two papers. Recent papers such as that of Stratton (1943) have recorded small groups of cases or individual cases. Stratton records the occurrence of this phenomenon in cases of carcinoma, bronchiectasis, jaundice and anæmia. Several recent papers have mentioned that persons showing this phenomenon also often show a very high sedimentation rate of the red blood corpuscles, and it has been suggested that the two conditions have a common cause. We have found, however, that persons with a very high sedimentation rate may not show auto-hæmagglutination. Recently two or three publications have appeared in which has been reported the occurrence of auto-hæmagglutination after and apparently as the result of the administration of drugs of the sulphonamide group.

Dr. Parekh's article in our present number records one such case. One other case has also been reported in which after sulphonamide administration the red cells contained an abnormal agglutinin (Levine and Katzin, 1938, quoted by Wiener, 1939).

Until recently, the phenomenon has attracted little attention in India, and we have not been able to trace a single original contribution to the subject in this country. During the last few months, however, several reports, both oral and written, have reached us regarding the occurrence of this phenomenon in numerous cases of malaria seen in the army, and one correspondent has even recorded that most cases of malaria show this phenomenon and has even suggested that it is of diagnostic value. Such reports, however, have not been published. Now from another source comes Dr. Parekh's article on the subject of auto-agglutination seen in a patient in a Bombay hospital (see page 527).

It is quite obvious that numerous cases of this phenomenon are now being seen in India, and that it is attracting very considerable attention. The phenomenon may interfere with many procedures which are commonly carried out; it may make it difficult to make blood films; it may make a blood count impossible; it may make blood grouping difficult if the method of pricking the finger is used; it may interfere to some extent with blood transfusion work. For these reasons we are very glad to have the opportunity of drawing our readers' attention to this phenomenon and of discussing the matter.

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One striking fact is that, after a fairly thorough study of literature on this subject, we have found no reference whatever to the occurrence of this phenomenon in malaria. Yet we are assured by competent authorities that large numbers of such cases are now being seen in the army. We have had the opportunity of studying one such case, and the phenomenon was certainly present, although the titre of the agglutination was obviously low. It is hoped that a further study of such cases will be possible. We here discuss the more general aspects of the question.

The article by Cohen and Jones is reprinted on page 564, and all interested in this subject should read this article carefully. The article by Boxwell and Bigger covers to some extent the same ground as that of Cohen and Jones, but it discusses in greater detail the nature of the phenomenon. Their definition of the phenomenon has been quoted above. Regarding the differentiation between pseudo-agglutination and auto-agglutination they state as follows:—

'To Landsteiner must go the credit for having clearly differentiated pseudo-agglutination from auto-agglutination. Pseudo-agglutination is excessive rouleau formation. In it the well-known arrangement of the cells into piles is observed, while in auto-agglutination the grouping is quite irregular. Further differences are that slight dilution of the serum (to a third or a quarter) inhibits pseudo-agglutination but not, usually, auto-agglutination, and also, and most important, in true auto-agglutination the condition is reversed by heating to body temperature (that is, a uniform dispersal of the cells is observed when those which have agglutinated at air temperature are heated to 37°C.), while in pseudo-agglutination the condition of clumping is even more marked at body temperature than at that of the air.'

The phenomenon therefore seems to be quite a definite one, one that has been known for many years, reported by many workers, and thoroughly studied by a considerable number. Workers in India who encounter this phenomenon should therefore realize that they are not encountering anything new. The writers in the literature of the subject are unanimous in the opinion that this phenomenon does not occur at body temperature and, therefore, is of little direct significance to the patient himself, and contributes nothing directly to disease processes with which it is usually associated. It is only when the blood is studied outside the body that the phenomenon appears. It has been suggested, however, that this phenomenon may occur in the body, particularly in the superficial vessels when the body is exposed to cold, and the possible bearing of this phenomenon on paroxysmal hæmoglobinuria is obvious. In this condition auto-hæmagglutinins as well as auto-hæmolysins have been reported and it is possible that the agglutinin and lysin are one and the same substance. Our correspondent has not only found auto-agglutination common in malaria, but has observed certain changes in the superficial vessels, particularly those of the conjunctiva, and attributes these changes in the vessels to

auto-agglutination going on in them. This is not impossible.

It appears very doubtful, however, if the occurrence of this phenomenon in malaria, which is now being very commonly reported, does contribute anything to the causation of any of the major symptoms of malaria. This suggestion has, however, been made by one or two correspondents.

It is interesting, however, to observe that certain observations on this matter have been made in experimental malaria in canaries. An article on malaria agglutination has recently been published by Lack and an extract of this article is published in our present number, page 566. The circulation of the wing web of canaries was observed under the microscope and agglutination was observed, but it is not clear at what temperature these observations were made. The abstract records that intra-vascular agglutination had previously been described in experimental malaria in monkeys by Knisely and co-workers, and the abstract ends: 'the phenomenon presumably occurs in man.' This is a very interesting point, but it can be definitely stated that, while recent reports indicate that in certain areas of India which are notoriously malarious auto-agglutination as defined by Boxwell and Bigger is not uncommon, it appears very doubtful whether even there it is of any clinical importance. Moreover in the thousands of blood films, thin and thick, that are studied in other areas of India every year at such centres as the Calcutta School of Tropical Medicine, this phenomenon has very rarely been seen, and the difficulty in making a blood count, which is the circumstance which usually draws attention to the phenomenon, is practically never encountered. We feel, therefore, that the soundness of the idea that this phenomenon is characteristic of malaria and contributes to the causation of certain manifestations of malaria does not rest on a sound foundation. More evidence on this point is needed before this idea can be accepted. Even if it can be caused by malaria in the body, it must be confined to the superficial vessels. Auto-agglutination at body temperature has never been described and if it occurs it would certainly be incompatible with life.

It should be pointed out that difficulties in blood grouping and in blood transfusion work caused by auto-hæmagglutination can be overcome. If auto-hæmagglutination is seen when blood is taken on the slide by the pricking method, blood should be taken from a vein into citrate or oxalate, and at once be centrifuged; the separated and washed blood cells can then be grouped with no difficulty. The plasma or serum cannot be used for blood-grouping tests unless the auto-hæmagglutinin is first removed by absorption, by leaving it in contact with red cells overnight in a refrigerator, and then separating it.

Special Article

THE ORGANIZATION OF THE CALCUTTA BLOOD BANK : DONOR AND COLLECTION SERVICE

By D. N. CHATTERJEE

(From the All-India Institute of Hygiene and Public Health, Calcutta)

THE extension of the war made it imperative to start a blood bank on modern lines for the processing of serum or plasma in India. The Government of India took a lead in the matter and early in January 1942, the Calcutta Blood Bank was established at the All-India Institute of Hygiene and Public Health in collaboration with the Bengal Branch of the Indian Red Cross Society. This was the first blood bank opened in India to process serum in quantity. The Bengal Branch of the Indian Red Cross Society had been running a blood bank to meet the peace-time civilian requirements. This, however, was on a very small scale and provided less than 200 transfusions in 1941. The expanded blood bank was placed under the jurisdiction of the existing committee of the Red Cross. Blood banks have now been established in different provinces in India. Some of the workers in these other blood banks were trained at the Calcutta Blood Bank.

It has been emphasized by organizers of blood banks that the success of an organization of this kind depends on two main factors—recruitment of donors and bleeding them efficiently. Recruitment of volunteer blood donors from amongst the civilian population of this country has been found a difficult problem mainly on account of the newness of the procedure and natural apprehension regarding the after effects of such an operation. The method of recruitment adopted therefore had to be of a type different from that in other countries where people are more 'blood conscious'. Our campaign for the enrolment of volunteers therefore began with lectures in public places, practical demonstrations of blood letting, distribution of educative pamphlets in different languages, newspaper publicity in the name of leaders in the local newspapers and special articles on the blood bank. Although this produced some result it was not enough to give us a steady flow of donors which is essential for the efficient working of a bleeding unit.

It has been our experience that the most effective way of enrolling donors is by repeated personal interviews with heads of firms, factories, clubs, etc. Talks are given to departmental heads and to groups of employees, explaining the need for blood, the harmlessness of the operation and requesting them to give a lead themselves and thus set an example to the staff serving under them. When a group of persons is ready to donate blood, a practical

demonstration of blood letting is given in that place by bleeding the volunteers in their own office to allow others to watch the effect of the operation. Donors who have given their blood two or three times are also requested to enlist the sympathy and support of their friends and acquaintances and get them to volunteer as blood donors. Opinions of donors are asked as to any defect in the arrangements of blood collection, and attempts are made to rectify those according to their suggestion. The medical profession is requested from time to time to lend their support to this organization by assuring their clients who come to them for advice about the harmlessness of the operation. In making bleeding appointment with donors, every care is taken to inconvenience them little. It has been the principle of this bank to send out bleeding teams to the places wherever a group of donors is available, to minimize the amount of time lost from work by employees and to obviate the necessity of people in the outlying districts coming relatively long distances to the central place, particularly at a time when transport is so difficult. In order to attract donors, a metal badge is given to each donor on the centre of which his blood group is stamped. When donors give their blood more than once, an additional bar is given on which the number of times he has donated blood is indicated. At the tenth donation a silver badge is given to the donor. The badge is very much appreciated by the majority of donors.

General organization of the clinic

The Calcutta Blood Bank has been divided into four sections, the Office, Clinic, Processing Laboratory, and Sterilization and other laboratory measures. In a work of any volume this is essential. The office registers the names of the donors and is responsible for making appointments for their bleeding at a mutually convenient place and time. Such appointments necessarily have to be made in advance in order to provide the staff with regular work. This necessitates drawing up of a daily time table (Appendix I).

The processing laboratory pools the serum from the blood collected and filters it. The drying section is a part of this section. The sterilization of equipment and laboratory tests such as blood grouping and Kahn reactions are done by the Microbiology Section of the Institute.

The clinic is provided in advance with a copy of the time table (Appendix I) and arrangements are made for bleeding the donors either at the main clinic in the All-India Institute of Hygiene and Public Health or at places suggested by the different groups of donors. For convenience to the donors, the Calcutta Blood Bank has been doing 75 per cent of its collections outside the main clinic. Teams are sent out to different places all over Bengal according to demands. A team consists of a medical officer,

a dresser and a peon. A preliminary inspection is made of the facilities available in the place where the bleeding clinic is to be set up, and if and when necessary, furniture for the bleeding clinic as well as refreshments given to the donors after bleeding are sent out with the team.

The bleeding clinic

The clinic at headquarters is provided with a reception room where the donors wait for a few minutes before they are ready for bleeding. During this period the receptionist posted there takes their weight and fills in their names and addresses on a card (Appendix II). The clinic is air-conditioned to maintain a constant temperature of 78° to 80°F. It is divided into different bleeding cubicles. The arrangement of bleeding in separate cubicles is more suited for the clinic at the headquarters on account of individuals attending the clinic who do not like the idea of being bled before a complete stranger. Furthermore, any reaction after blood donation does not affect other donors adversely. When donors are bled outside the central clinic, since they happen to be mostly in groups, they are usually bled side by side in full view of each other. This arrangement allows larger groups to be handled quickly by a single officer with additional assistance. The central clinic usually deals with such small groups that it has never been possible or necessary to follow this technique. After the individuals have been bled, they are taken to the rest room where they are served with a cup of tea, coffee or cold drink with biscuits or cakes. The rest room is away from the waiting room so that donors waiting to be bled are not required to mix with donors who have already been bled. This is most essential in avoiding epidemic syncope in donors. No effort is spared to make the general atmosphere of the clinic pleasant, and the blood bank staff is instructed to keep up the spirit and confidence of the donors by talking to them on subjects, other than blood donation, in which the donor seems to be interested. To further divert the attention of the donors, a radio has been installed at the clinic.

TABLE I

Blood donors from different groups of population up to 15th May, 1943

	Calcutta and suburbs	Outside Calcutta
Offices and Institutions ..	5,414	..
A.R.P. and First Aid Posts ..	1,144	..
Police ..	939	1,442
Railways ..	640	762
Jails ..	752	154
Tea gardens	5,685
Military ..	7,406	5,126
Miscellaneous ..	1,131	2,982
	17,426	16,151

Out of these only 5,458 have been bled at the headquarters clinic.

TABLE II

Distribution of donations amongst military and civilians

Indian civilians ..	16,540
Other (European, Anglo-Indian, Chinese, etc.) civilians ..	9,978
Indian military ..	5,839
Other military ..	6,693
	39,050

TABLE III

Frequency of donors who donated blood more than once and their distribution amongst Indians and others

	Total number of donations	Indians	Others
Total donation up to 15th May, 1943 ..	39,050	22,379	16,671
1st donation ..	33,577	21,372	12,205
2nd ..	3,075	777	2,298
3rd ..	1,194	154	1,040
4th ..	545	41	504
5th ..	336	20	316
6th ..	183	9	174
7th ..	101	5	96
8th ..	38	1	37
9th ..	1	..	1
	39,050	22,379	16,671

Technique of bleeding.—As soon as a donor arrives in the bleeding cubicle, the medical officer in charge requests him to take off his coat, open his shirt, roll up his sleeves, and loosen his shirt neck band and belt. He is then requested to lie down on the examination table and a general physical examination of his health is done by the medical officer (Appendix II). Both male and female donors between the ages of 18 and 60 are accepted. The physical fitness to donate blood is determined after taking a short history of recent illness, determination of the blood pressure, general examination of the heart and lungs, and, where indicated, an examination of the spleen and liver. A donor with an obvious temperature or with a systolic pressure of less than hundred is not accepted. Persons with a history of malaria are accepted as donors provided there is no enlarged spleen, no obvious anaemia and the last attack was a month previous to donation. Persons with a history of allergy also may serve as blood donors since the serum collected from such cases is pooled along with the other normal bloods and consequently is so diluted that the allergic factors are not transmissible to the recipients. Since the blood bank here is mainly processing serum and collecting very little blood for whole blood transfusion, the question of filaria and syphilis is eliminated since the blood collected is stored at such temperatures that spirochaetes cannot

survive and the filtration of the serum gets rid of the microfilaria. Persons with organic heart disease or with an irregular pulse are rejected. A special note is made as to the maintenance of weight by donors coming for repeated donations, and if at any time they show any marked loss of weight they are questioned as to the reasons for this loss and if there is any doubt as to the fitness of the donors, they are asked to come after two months. Persons with a very high systolic pressure are accepted as blood donors, but the quantity of blood taken is reduced.



Fig. 1.—A donor being examined before bleeding.

The bleeding set.—The bleeding set consists of a semi-pressure rubber tubing 15 inches long with an internal diameter of $3/16$ inch and wall-thickness of $1/20$ inch, at one end of which there is a 2-inch cupro-nickel silver cannula attached, and at the other end a needle adaptor to which a 13 to 14 gauge venepuncture needle is attached. These are sterilized together minus the venepuncture needle in a dressing drum in the autoclave. The venepuncture needle is separately sterilized in olive oil at a temperature of 160°C . for 10 minutes and put into individual conical sterile glass containers. Before use the needles are taken out with aseptic precautions and fitted on the adaptors in the bleeding set. The blood is collected by 'closed system' requiring very little manipulation for the assembly of the set. The bottles used for bleeding are the Medical Research Council pattern made of neutral glass with a capacity of 540 c.cm. waisted in the middle. A partial vacuum is created in the bottles during the sterilization by keeping the caps loose before they are put inside the autoclave and tightening the caps while hot as soon as they come out of it. This vacuum inside the bottles is about 10 to 15 inches which is sufficient for a free flow of 400 to 500 c.cm. of blood. The rate of flow of blood aimed at is about 100 c.cm. per minute. When necessary additional vacuum can be produced inside the bottle by pushing in a Higginson's syringe through the second hole and sucking out air.

A prominent vein in the elbow region, usually the median basilic, is selected. Other veins may be used if necessary. The site of venepuncture is cleaned first with 70 per cent alcohol followed by 7 per cent tincture of iodine and then with ether. The sphygmomanometer cuff folded to one half its width is applied to serve as a tourniquet to make the vein prominent and facilitate venepuncture. The cuff is applied in the reverse position so that the tubing is away from the site of the venepuncture. Usually the pressure on the arm is maintained at 80 mm. of mercury. No local anaesthetic is used since the size of needle is smaller than that used at other banks and as 'vacuumized' bottles are used, this size of needle is quite efficient for taking out the requisite amount of blood from every individual. These needles are particularly useful for drawing blood from Indians since they have much smaller veins than Europeans. The needles are kept particularly sharp to cause the minimum amount of inconvenience to the donors. Cutting down on a vein is never employed and medical officers are instructed not to make more than one attempt to get into the vein without the consent of the donor. In case of a failure not more than two punctures are made at any one time. No sterile towels, masks, gloves or special gowns are used excepting for clean overalls worn by all the workers in the clinic. Before proceeding with the venepuncture the medical officer cleans his hands with soap and water and then applies an antiseptic lotion such as lysol or perchloride while the dresser sterilizes the site of the venepuncture.

Now the medical officer introduces the needle with the eye of the needle pointing downwards into the selected vein, and the assistant pushes the cannula at the other end through the rubber washer on the cap of the bleeding bottle. It is noted whether the blood is flowing freely or not. Sometimes a little manipulation of the needle is necessary to get free flow of blood. If the flow gets weak due to lack of vacuum in the bottle, supplementary vacuum is produced through the second hole on the cap of the bottle after flaming the needle attached to the Higginson's syringe. A few strokes of the syringe is enough to restart the flow. It takes about 5 to 6 minutes to extract 500 c.cm. of blood from a donor by the foregoing method. The flow is maintained by asking the donor to slowly open and close his fist in which he holds a wooden grip. If during collection there is a fluttering sound at the site of puncture, the blood flow is stopped for a few seconds and then allowed to run slowly. The fluttering is caused by attempts to draw the blood faster than the vein can be filled. This is undesirable as it has a definite tendency to haemolyze the blood.

After the requisite amount of blood has been withdrawn, the cannula end of the rubber tubing is tightly pinched by the assistant while the medical officer takes out the needle after releasing the tourniquet. The latter is an

important step since if the pressure is left it produces a hæmatoma causing considerable inconvenience to the donor. The blood left in the rubber tubing is collected in a small phial for a Kahn test after putting a few drops of serum for grouping in a test tube containing 2.5 per cent sodium citrate in normal saline.

which they are stored in the cold storage having a constant temperature of 3° to 5°C.

In collecting blood for the purpose of processing serum, it is essential that every possible precaution should be taken to prevent contamination of the blood at the time of collection. All the bleeding sets, the bleeding bottles and

TABLE IV

Summary of donors attending different clinics from 6th February, 1942 to 15th May, 1943

Month	Number of donors who came to donate	Number of bleeding days	Number rejected	Number bled	Blood obtained, c.cm.
1942—					
February	669	24	106	563	158,395
March	1,293	26	83	1,210	335,815
April	1,839	25	136	1,703	541,665
May	1,972	26	143	1,829	568,015
June	1,717	26	109	1,608	464,690
July	2,098	26	113	1,985	680,505
August	1,597	26	134	1,463	486,660
September	1,550	26	98	1,452	474,555
October	1,870	24	51	1,819	608,315
November	4,053	25	284	3,769	1,197,390
December	3,709	26	209	3,500	1,056,315
1943—					
January	3,090	25	108	2,982	960,285
February	3,807	23	205	3,602	1,043,225
March	4,556	27	203	4,348	1,239,985
April	5,568	24	209	5,359	1,509,315
May (15th)	1,922	13	64	1,858	527,535
TOTAL	41,310	392	2,260	39,050	11,853,665

The site of venepuncture is pressed with a wad of cotton for a few minutes to stop bleeding. The puncture is sealed with collodion. After the holes on the washer of the cap have been sealed with molten paraffin, the blood bottle is slanted on a wooden rack to allow separation of serum. The donor in the meantime is served with a cup of tea or coffee and is encouraged to rest for 10 to 15 minutes. The blood bottles are kept at room temperature for an hour, after

needles are meticulously cleaned and autoclaved. Drums used for sending out bleeding sets are sealed so that no one can open them except the medical officer or his assistant. All palpation for difficult veins is avoided. The venepuncture needle is not used for more than a single penetration of the skin, or if it is used it is resterilized before a second puncture. All care is taken to transport the blood and separate the serum as quickly as possible. Samples of blood collected by this technique at the Calcutta Blood Bank have been put up for sterility tests from time to time and found to be sterile. No bactericidal or bacteriostatic agents are used for the preservation of the blood.

Care of the bleeding set.—For the sterile collection of blood it is essential that the bleeding sets should be cleaned immediately after use. Within a few minutes of its use, the set is flushed first with tap water by forcing water through the tube by means of a Higginson's syringe. The venepuncture needle is also flushed with tap water; at the same time clots are removed by passing a stilet through the needle. The sets are now dis-assembled and remaining clot inside the tube is removed by passing a metal rod through the tube, at one end of which a piece of linen is attached. The set is again flushed and boiled in normal saline. The sets are re-assembled and tested for leaks in the



Fig. 2.—Some of the tea garden donors having refreshments after blood donation.

system by passing 2.5 per cent sodium citrate in pyrogen-free normal saline. A small amount of citrate is left in the set to prevent clotting of blood at the time of collection. The venepuncture needles are thoroughly cleaned with water forced through by means of a hypodermic syringe, are boiled in olive oil at 160°C. for 10 minutes, and are put into small conical sterile glass tubes.

Mobile units.—The mobile units are prepared to go anywhere in Bengal for the collection of blood. Blood has been collected from places as far away as Ranchi, Ramgarh and Bilaspore in Central Provinces. Bleeding operations have been carried out in offices, clubs, factories, jute mills, tea gardens, private houses, colleges, A.R.P. depots, hospitals, shops, and even on steamers. Sometimes the blood had to be transported by most difficult roads and in all seasons. Every kind of transport available in India has been utilized for this purpose, including bullock carts and coolies. The loss of blood transported from difficult places, such as the interior of the Alipore Dooars tea gardens, due to breakage of bottles, hæmolysis or contamination has been negligible. Wherever a sufficient number of volunteers (15 to 20) are available, a team consisting of a medical officer, a dresser and a peon is sent out for collection of blood. A time-table is sent in advance to the organizer to draw up the programme according to the convenience of the individual donors. Where possible a preliminary survey is made for the selection of the bleeding room. A clean, well-lighted room, preferably provided with fans and with water at hand, is selected. Arrangements have to be made for supplying light refreshments and drinks for the donors; this is done by the organizer locally or else provisions are sent out with the team from the blood bank. The team is provided with the necessary equipment and folding beds, tables and linen. Locally the teams are transported by the station van.

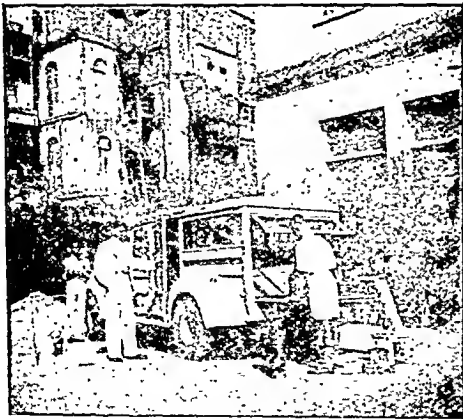


Fig. 3.—A team getting ready to leave for an outside appointment.

When the teams are required to work outside Calcutta, the local organizers inform the blood bank 7 to 10 days before the scheduled time, and the number of donors from whom the blood

has to be collected is stated. As a sufficient supply of ice is not available at most of the outstations, arrangements are made from Calcutta for a regular supply of ice to the teams at their places of work. A peon is sent every day with fresh sterilized apparatus; he brings back the blood collected at the particular station packed in ice boxes specially prepared for this purpose. When boxes of blood arrive in Calcutta, the temperature of the box is checked and the absence of hæmolysis and contamination is confirmed.

Refrigeration.—Blood collected at the Institute clinic is under ideal conditions since the bleeding clinic is air-conditioned. The collected blood is stored in cold storage within an hour of bleeding. This maintains a temperature of 3° to 5°C. The blood is transported from outstations in specially designed insulated ice boxes. Inside these boxes are galvanized iron trays for holding twelve blood bottles covered with a hood to prevent wetting the paper caps on the top of the bottles. Ice is packed all round the tray before starting bleeding so that the bottles are chilled, and at the end of the day's work more ice is put in before sending the boxes to headquarters with instructions to the peons to keep a watch on the ice and when necessary to replenish that. It has been found that blood transported in this way seldom exceeds a temperature of 5° to 10°C. A special box has been devised in which the temperature is maintained at 4 to 5 degrees centigrade without any replenishment of ice for 24 hours.

Laboratory examinations.—In view of the recent work showing that *Treponema pallidum* does not survive at a temperature of 5°C. for three days, the transmission of syphilis can safely be ruled out as the collected blood here is kept at that temperature. This blood bank has therefore discontinued the routine application of the Wassermann or Kahn reactions. These are only undertaken on special demand for such tests from a particular group or individual. The blood of all donors is grouped however when donating for the first time and rechecked at the second donation and every one is informed of his or her group to facilitate immediate transfusion of whole blood if needed.

TABLE V

Causes of rejection with their percentage

Unfit	1,529 or 3.90%
Missed vein	146 or 0.35%
Deep veins	181 or 0.44%
Failure of instrument	145 or 0.35%
Small quantity of blood taken	259* or 0.63%

* Less than 75 c.cm. could be drawn from these cases.

Reactions.—One of the greatest setbacks in the recruitment of donors is occasional syncopal attacks sometimes met with amongst blood

TABLE VI
Amount of blood rejected for various reasons

Blood received	Rejected	CAUSES FOR REJECTION			
		Serological tests positive	Hæmolyssed	Chylous	Other causes
11,853 litres	502 litres	159 litres	80 litres	221 litres	42 litres

donors. Although simple in itself, it occasionally shows such alarming symptoms, particularly to the lay public, that it scares away many a prospective donor who happens to have seen such an incident. The reasons for these attacks have not been fully explained, but amongst others the psychological factor is considered to be the most important. Exhaustion and dehydration due to sweating may be contributory factors. A detailed study of the condition is being made which will be reported later. It is obvious how essential it is to prevent such attacks. Much can be done by general management of the donors. The clinic is arranged in such a way that no chance is given for the waiting donors to meet the donors who have already been bled or are being bled. If a donor arrives in the clinic exhausted on a hot day he should be asked to rest for a few minutes and be given a cold drink before being bled. There should be the minimum amount of delay in taking the blood, so that everything should be kept ready. Any waiting serves to increase a donor's natural apprehension. His attention is distracted from what is being done by keeping a running conversation with him on matters of general interest. This results in the relaxation of the emotional tension of a nervous person and in averting impending attacks of syncope. A reduction of such attacks in a particular group of donors always helps in recruitment of further donors from that group and increases the chances of their becoming regular donors in future. The signs of such faints are flushing, pallor, sweating, nausea and vomiting, slow thready pulse, occasionally clonic type of convulsions and rarely incontinence. The best way of dealing with such cases is to take away the pillows from the head, and lower the head of the couch where possible. The donor is assured that it is nothing serious and as little fuss is made about it as possible. Mild stimulants such as smelling salts may be used. The reactions are usually of such a mild nature that injections of stronger stimulants such as adrenalin are very rarely needed. The donor is left on the bed so long as he is not well enough to walk to the rest room. It has been found that syncope is even less common among Indian donors than among European donors. This matter is to be discussed in a future paper. An analysis of syncopal attacks amongst the donors reveals that 4 per cent of the donors fainted. This figure is quite in keeping with

the figures obtained elsewhere. About 90 per cent of these syncopal attacks however were of the milder type accompanied with pallor, sweating and a little nausea in some cases but with no actual loss of consciousness.

Protection to the donors.—It has been observed in the different blood banks that individuals donating a large amount of blood at fairly frequent intervals do not suffer much ill effect, but it should be remembered that there may be a few who may not have an efficient hæmopoietic system to regenerate blood as quickly as is needed. It is necessary therefore to check the hæmoglobin value of regular donors from time to time, and, when necessary, to give them treatment for any anæmia that may have developed as a result of blood donation. As a routine method, this blood bank is estimating the hæmoglobin value of all donors coming for the fourth time onwards. It is the practice here not to bleed persons with a hæmoglobin value below 14.43 grammes or 105 per cent in males and 13.06 grammes or 95 per cent in females on the Hellige scale. Persons whose hæmoglobin value is found to be below normal are advised to come back for re-examination of their hæmoglobin value, and in the meantime are treated by administration of iron.

TABLE VII

Total number of donors in whom hæmoglobin was estimated—360

	European males	European females	Indian males	Indian females
Normal ..	176	108	68	8
Below ..	3	18	9	Nil
	1.7%	16.6%	13.2%	Nil

Conclusions.—The Calcutta Blood Bank has now bled 33,577 donors. About one-third of the donors have been provided from the military and the other two-thirds consist of civilians, both European and Indian. The tea estates alone have produced about 6,000 donors, the majority of whom are Indian labourers. On the whole, the response from the Indian civilian although encouraging has been comparatively poor. This is due to apathy and natural apprehension as to the results of such donation on the health. With greater education on the subject and realization of the importance of treatment with

blood and blood substitutes, it will be possible to overcome the disinclination of the general public to volunteer to donate blood. More frequent use of blood and other blood substitutes will go a long way to stimulating general interest on the subject.

At present there is a certain amount of confusion on the mind of the medical profession as to the methods for obtaining stored blood or serum for transfusion purposes. The bank has issued serum requisition forms to most of the A.R.P. hospitals in the city as well as in different parts of Bengal, and whenever requisitioned, they have been provided with serum for emergency use. The bank has made arrangements that during air raids further stocks of serum can be obtained on demand from the bank, where a responsible officer is on duty. In addition to this, the Calcutta Blood Bank has a Civil and Hospital Transfusion service which operates in the School of Tropical Medicine, Calcutta. It maintains a 24-hour service for the supply of donors of fresh blood, stored blood and serum to hospital patients. War has given a great impetus to treatment of shock by transfusion of blood and its substitutes, but its importance in peace time is no less, and this is the opportunity for organizing the medical profession and the general public. With this end in view the Calcutta Blood Bank is organizing the training of medical officers from different hospitals in Bengal in resuscitation methods, the main function of whom will be giving transfusions. These officers can be put on charge of a permanent transfusion service in their own hospitals.

In an activity of such a nature, it is the responsibility of the organizers to afford sufficient protection to the donors. For this purpose the blood bank has an advisory board with two eminent physicians and two eminent surgeons to advise on standards of physical fitness of donors and general management of the clinic. As already mentioned no donor is bled unless it is ascertained that the person is in a fit condition to donate blood. A check is made on the weight and blood pressure of all individuals coming for re-donations and any loss of weight is carefully enquired into. Hæmoglobin

tests are done from fourth donations onwards, and those found below normal are rejected and given proper treatment. That the methods of selection are efficient can be judged by the fact that out of 33,577 donors bled there have been reports of ill health from not more than half a dozen persons. One has to be very careful on this point as otherwise it very materially affects the recruitment of donors. There have been 1,529 rejections due to physical unfitness. Only two cases of minor injury occurred since the beginning of this bank, caused by falling in syncope; one patient clipped a tooth and the other sustained a contusion on the forehead. No one has so far reported infection at the site of venepuncture. A peculiar case was reported by one of the donors who developed a varicosity of the vein at the site of venepuncture associated with intermittent venospasm and consequent pain on the arm. The donor was admitted into the Medical College Hospital and was discharged cured. A few persons have complained of general weakness and lassitude after blood donations. Donors are called for re-donations once in nine weeks. A study is in progress to determine the blood regenerating power of different individuals after repeated blood donations. Reactions such as syncope are avoided as much as possible by withdrawing smaller amounts of blood from nervous donors. The average amount of blood drawn from all nationalities is 280 c.cm. to 300 c.cm. Every individual is informed of his blood group according to the international classification, so that all the institutions co-operating with this scheme are automatically provided with a donor panel who in case of an emergency may be utilized for direct whole blood transfusions. The typing is done and re-check is done on all second donations and out of nearly 35,000 examinations discrepancies have not appeared more than in a dozen instances. It is however emphasized that in giving transfusion with citrated blood a cross matching should always be done to avoid any mistake.

My thanks are due to Dr. J. B. Grant, Director, All-India Institute of Hygiene and Public Health, for his kind interest and permission to publish this paper.

APPENDIX I

CLINIC APPOINTMENT

Date

Place	Doctor	Furniture	Lunch	Hour scheduled	No. of donors
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APPENDIX II

Name	No.
Private address	Business address
Phone	Phone

RECORD OF VISITS

Date	Quantity	Date	Quantity	Date	Quantity	Date	Quantity
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Information

(On the reverse)

PHYSICAL EXAMINATION

Age	Sex	Group	Condition of veins	No.
Physical exam.		Recent illness		General health
Weight	Heart	Lungs	Liver	Spleen
Edema of legs		Blood pressure	Sys.	
Lab. findings, W.R.		Dias.	Hæmoglobin	

Remarks :

Medical News

THE FACULTY OF TROPICAL MEDICINE
AND HYGIENE, BENGAL

The following students are declared to have passed the L.T.M. Examination, Session 1943.

Passed

(Arranged in alphabetical order)

1. Keshab Lal Baishya Saha, L.M.F., private practitioner.
2. Netai Pado Banerjee, L.M.F., private practitioner.
3. Shambhu Nath Banerjee, L.M.F., private practitioner.
4. Gana Nath Bose, L.M.F., private practitioner.
5. Debendra Nath Chakravartty, L.M.F., private practitioner.
6. Narendralall Chakravortty, L.M.F., Sub-Assistant Surgeon, Burma Government (on leave).
7. Hari Narayan Dutt, L.M.F., Medical Officer, Faridpur District Board.
8. Triguneswar Ganguly, L.M.F., Sub-Assistant Surgeon, Bengal-Nagpur Railway.
9. Baidya Nath Ghosh, L.M.F., Medical Officer, 9 and 10 Pits Colliery, Sodepore.
10. Durga Das Ghoshe, L.M.F., Assistant Medical Officer, Sathgao Tea Estate, Sylhet.
11. Basant Singh Grewal, L.M.F., private practitioner.
12. Sudhir Ranjan Mondal, L.M.F., private practitioner.
13. Robindra Narain Roy Chaudhuri, L.M.F., Assistant Medical Officer, Chengamari Tea Estate, Dooars.
14. Sudhanwa Kumar Saha, L.M.F., private practitioner.
15. Kedar Nath Sawhney, L.S.M.F., private practitioner.

16. Nalin Kumar Sen Gupta, L.M.F., private practitioner.
17. Bhupendra Narayan Talukder, L.M.F., private practitioner.

ROSS INSTITUTE OF TROPICAL HYGIENE,
INDIA BRANCH

At the annual meeting of the above branch, held in Calcutta on 26th August, 1943, Mr. C. K. Nicholl, Chairman of the Committee of Control, referred to the retirement of Sir Malcolm Watson, Director of the Institute in London, early this year, and to some of the activities of Dr. Ramsay and his associates in India. Though the work was chiefly confined to the control of malaria there were contributions by 'Ross Institute' men on other subjects too. For instance, Ramsay showed that yaws, and not syphilis as had previously been assumed, was the disease which was causing ravages among Assam Hill tribes. Hamilton showed that the eye-fly, which is responsible for epidemics of conjunctivitis, bred in the thatch of houses and bungalows. Fraser demonstrated the species of mosquito responsible for the transmission of filariasis in Assam. The anti-malaria measures adopted were principally the naturalistic ones which the work of the Institute has established to be the most effective and practicable. A very large number of medical men and malaria surveyors trained under Ross Institute auspices are now working with the Allied Forces in Assam, Middle East, West Africa and elsewhere, and great assistance is being rendered in vital Eastern Frontier areas. It has now been proposed to set up a branch of the Ross Institute in South India.

Public Health Section

THE PRESENT STATE OF OUR KNOWLEDGE OF SOIL AND GROUND WATER POLLUTION

By BRIAN R. DYER
and
T. R. BHASKARAN

AN adequate method for the safe disposal of human excreta is perhaps the most important problem which confronts rural sanitarians and public health workers. With the recognition of water as the carrier of many of the filth-borne diseases, more emphasis has been laid in recent years on the extent of soil and ground water pollution in deciding the sanitary and health protective values of these methods. A certain amount of research has already been carried out on this problem, and an attempt is made in the following brief review to critically examine the work so far done on this account.

Soil pollution

Spread of infection through soil pollution has been studied from very early times. Bowditch in America and Buchanan in England first observed that spread of certain diseases has something to do with dampness of soil. Petten Kofor and later on Ballard (1887) associated the spread of enteric fever and diarrhoea with certain soil conditions; they found that these specific organisms grew well under these conditions and thereby spread disease. The chances of spread of pollution through soil are largely dependent upon the life of the pathogenic bacteria under the conditions which they will encounter in soil and septic medium.

With the advance in the science of bacteriology, attention was, therefore, directed towards studying the viability of organisms, especially the intestinal pathogens, in soil, faecal discharge and septic medium.

Viability of the intestinal organisms in soil.—Houston (1897-1902), Chick (1900-01) and Horrocks (1903) found that *B. coli* was generally absent in virgin soil; but when pure cultures of these organisms were added to soil it persisted from 6 to 8 weeks. Typhoid and dysentery organisms have also been studied by a number of workers (Kliger, 1921) in regard to their viability in the soil. Although there was great divergence in the results, the following broad conclusions may be drawn from this work. The character of the soil, moisture and temperature seem to be the most important factors in determining the viability of these organisms in soil; peaty soil was found to be quite unfavourable to their growth; viability was greater in sterile than natural soil; the viability varied from 12 to 30 days in dry soil and 40 to 90 days in wet soil.

These pure culture studies have only a limited direct bearing on the field problem. It is well known that freshly isolated strains are less resistant than old stock cultures. Working with soil to which sewage had been added, Houston (1897-1902) found that there is a keen struggle between the natural soil flora and the foreign organisms, and that the former soon gain the upper hand.

More recently Kliger (1921) worked on this problem in much greater detail. He carried out experiments with both *B. typhosus* and *B. dysenteriae* organisms in pure cultures as well as with faecal emulsions placed in the soil. His results generally confirmed the previous work. In moist soil (pH 6.6 to 7.4) these organisms survived up to 70 days, whereas when the soil was dry the bacilli were not recovered beyond 15 days. In an acid soil (pH 4.8 to 6.5) 90 per cent of the organisms died out within the first 10 days and the remaining did not survive beyond 30 days. The survival period of these organisms was greater nearer freezing temperature (4°C.) than at higher temperatures. He also showed that the antagonistic action of the soil organisms was mainly due to the change in reaction of the medium and the inhibitory substances elaborated by them. From all this work it would appear that moisture and reaction are the most important factors which determine the viability of the intestinal pathogens in the soil; and under the most favourable soil conditions these organisms may survive not more than 3 months.

Viability of intestinal organisms in faecal discharge.—The earlier work on this aspect of the problem mostly centred round *B. typhosus*. The results showed that typhoid bacilli survived in the excrement from 10 to 30 days while the dysentery organisms persisted for a much shorter period. Kliger's experiments confirmed the previous work, although the survival period recorded by him was much shorter; he also showed that these organisms survived longer in solid than liquid faeces. He carried out detailed studies on the dysentery organisms also and showed that the Flexner type survived from 3 to 8 days while the Shiga bacillus could not be isolated from the excrement even after the second day. He extended his studies to the field, simulating actual conditions in a pit, and more or less confirmed his laboratory observations.

Viability in septic fluids.—Since the introduction of septic tanks for disposal of human excreta, much attention has been directed towards determining the viability of intestinal pathogens in septic tank fluids. The general conclusion from all this work seems to be that the typhoid organisms may survive in septic material as long as 14 days, but the larger proportion of them die out within the first 3 to 6

days. Kliger's experiments showed that these organisms die out rather rapidly in septic material; the typhoid organisms survived up to 5 days, the Flexner type of dysentery about 3 days and the Shiga bacillus for a very short time. Change in reaction of the medium and the presence of certain antagonistic products of metabolism were the chief factors which determined the survival period of pathogens in septic fluids.

Penetration of bacteria in soil.—Spread of infection through soil pollution is also dependent on the ability of the pathogenic bacteria to penetrate through soil of different degrees of compactness. Most of the earlier work using chemicals have little bearing on this aspect of the problem, as diffusion plays no significant part in the penetration of living bacteria.

Pfuhl, Abbe and collaborators, Davies and Tyndal and others showed that bacteria could not penetrate through soil unless washed down by rains. Kliger conclusively showed that pathogenic bacteria introduced into soil did not by themselves spread laterally or in any other direction except when they are carried by water. He also showed that in certain pervious soils, water may transport these bacteria through a depth of at least 2 feet in the course of 3 weeks; in compact soil the bacteria do not appear to be carried through even 1 foot of soil. This is in close agreement with the later work carried out at Wilmington by the North Carolina Public Health Service and the work of Eijken and Grijns (1917) in the tropics. More recently, Caldwell (1938) has adduced further direct evidence on this point. Working with pits above the zone of saturation under different conditions, she has shown that intestinal organisms are confined to the depository except as they are mechanically carried by other agencies, primarily fluid flow, and pollution is essentially by gravity flow downward, if soils below are pervious. As far as bacteria are concerned, they do not penetrate into the soil, although hookworm does so. The inability of pathogenic bacteria to penetrate into soil, and the comparatively limited life in septic and soil media, would suggest that spread of disease through soil pollution is very limited.

Ground water pollution

The foregoing researches would indeed show that soil pollution by itself is of little consequence in the spread of disease; provided the quantity of water entering the latrine is controlled and the ground water level also does not rise to within a foot below the bottom of the latrine, the chances of spread of disease through privies dug in soil are quite insignificant. However under other conditions where latrines penetrate into the ground water, the extent of pollution may be quite an important matter.

In recent years, with the introduction of the bore hole latrine the extent of ground water pollution under different conditions has assumed added importance. The bore hole latrine

generally consists of a bore 14 inches to 20 inches in diameter and reaching a depth of 15 feet to 25 feet in order to penetrate the ground water; the latrine works on the same principle as the septic tank and in addition the soil in immediate contact with the latrine acts as a filter bed. Our present knowledge of ground water pollution is mainly based on the extensive investigations carried out with this type of latrine, penetrating into ground water.

Burr, Herring and Freeman (1903) record some experiments on this subject. They have shown that under certain conditions *B. coli* and other sewage bacteria may be carried through soil for long distances, while generally passage of polluted water at low velocities through a column of 25 feet of fine sand renders it safe for use. Investigations on similar lines have also been carried out by the Public Health Service at Wilmington. *B. coli* was found as far as 200 feet away from pit latrines reaching ground water. The United States Public Health Service through an experimental board directed by Stiles (1909) and Stiles and Gardner (1910) carried out research which showed that when plenty of water is present in the latrine, the area polluted may be large, and once the pollution reaches the ground water it may travel as far as 200 feet to 300 feet. They also record that in some cases pollution travels against the flow of ground water as well as with it. Stiles and collaborators (1927) have carried out further detailed investigations on this problem. Working in a sandy soil with slow moving water, *B. coli* was recovered at distances varying from 1 foot to 232 feet away from an experimental trench containing excreta. They also record in this later experiment that the travel of *B. coli* was only along the direction of flow of ground water.

More recently Mrs. Caldwell has attacked this problem in much greater detail. Her investigations conclusively showed that pollution flows only along the direction of flow of ground water and that the extent of pollution was different under different soil and ground water conditions. The experiments were carried out mainly under two sets of conditions, one where an impervious stratum closely underlay the boring and flow, and the second where permeable soils of considerable depth existed below the latrine.

Working with a bore latrine made in unconsolidated soils where an impervious stratum closely underlay the boring, Caldwell and Parr (1937) found that *B. coli* was carried 25 feet to 30 feet and chemical pollution 85 feet from the latrine. However, at the end of 3 months defence was formed, after which period *B. coli* disappeared and the chemical characteristic also diminished. In this experiment the nature of soil in the region of flow was coarse sand, and the ground water velocity varied from 3 feet to 8 feet per day.

With high rates of flow of ground water of the order of 10 feet to 13 feet per day, Caldwell

(1937) showed that *B. coli* was carried up to even 80 feet and gross pollution persisted between 40 feet to 60 feet from the latrine for over 16 months, after which period defence was formed and *B. coli* did not flow beyond 10 feet distance.

Her studies (1937) with the envelope pit privy further showed that in regions of high rates of flow it is possible to minimize the flow of pollution and safeguard the ground water by interposing a layer of fine textured soil around the latrine and reaching the ground water.

Where permeable soil of considerable depth existed below the latrine, Caldwell (1938) has adduced evidence to show that the path of pollution flow under these conditions was the resultant of interacting forces of lineal flow of ground water towards the discharge stream and variations in densities of effluent flow in comparison to the ground water. Initially, the pollution stream flowed 1 foot below the latrine and later to greater depth, extending to 7 feet in the course of 6 months. In lineal section the pollution stream described a curvilinear path for a distance by virtue of its density, and then as density diminished through dilution with flow, the upper and lower limits finally converged to zero. In a medium sandy soil, chemical pollution was detected up to 320 feet, with high intensities as 80 feet. *B. coli* flowed only to a much less extent than the chemical stream; initially, it went up to 10 feet in 4 months and later on *B. coli* was not recovered beyond 5 feet. Coliform organisms other than *B. coli* and atypical *B. coli* formed a large percentage of the surviving colon organisms. The bacteriological stream was narrower than the chemical stream, and flowed only to maximum 3 feet depth below the latrine.

Discussion

From the foregoing investigations and findings, it is quite conclusive that soil pollution by itself does not spread disease. Privies are quite safe in regard to sub-surface pollution provided they are properly constructed in soils free from cracks with at least a few feet (5 feet) of soil intervening between the bottom of the pit and the ground water.

However, under certain other conditions it has been shown that privies may be a source of real danger once the pollution from privies reaches the ground water for it may travel a considerable distance. The diversity in the results obtained in the ground water pollution studies would indeed show that the problem is not so simple as the earlier workers envisaged.

Soil is a complex medium and differs from place to place. The natural state of the ground water is also of varying composition, so that it is difficult to detect traces of pollution in it by simple analyses. The work carried out in the Punjab (Dyer's unpublished data) showed that rigorous statistical planning of experiments based

on the foregoing considerations is necessary to yield any data of fundamental significance. Work on these lines has not so far been carried out.

Nevertheless, the foregoing researches have adduced conclusive evidence on at least the following points in regard to ground water pollution: (a) pollution travels to any significant extent only in the directions of the flow of ground water, (b) with the initial flow of pollution the interstices in the soil are rapidly filled forming what is known as 'defence' which retards further flow of pollution; and (c) chemical products travel greater distances than the bacterial. The extent to which pollution will flow under different soil conditions is still uncertain. From the researches already carried out it would appear that the fundamental factors which determine the extent of pollution flow are the nature of the soil medium, the velocity of flow of soil water and the mechanism of formation of defence *in situ* in the soil. So far there has been too meagre relative data on these points to draw any general conclusion. Further work on these aspects of the problem may lead to simple methods of determining the extent to which ground water pollution from privies may be a source of danger.

Perhaps the most important problem of rural sanitation in India is firstly the provision of a suitable latrine to every villager. It should necessarily be cheap, easy to instal, cost little for upkeep, and need little attention. Bore hole latrines satisfy all these requirements. In recent years, many bore hole latrines have been installed in different parts of the world. In India also, it is being introduced as a forward public health measure. The extent to which these latrines will endanger shallow well water is uncertain. Owing to the paucity of data on this point, there is still a certain amount of legitimate diffidence among the public health men in the country in adopting this measure.

Further detailed investigations on these and allied aspects of the problem are being carried out under different soil and ground water conditions in the Punjab and Bengal by Dyer and Bhaskaran, the results of which will throw further light on the foregoing aspects of the problems.

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Current Topics

Auto-Hæmagglutination in a Case of Pernicious Anæmia, with Subacute Combined Sclerosis

By H. COHEN, M.D.

and

A. R. JONES, M.B.

(From the *Lancet*, Vol. II, 25th October, 1924, p. 853)

THE agglutination of a person's red blood corpuscles by his own plasma or serum—i.e. auto-agglutination—would appear from the literature to be of rare occurrence in man. The case we record below was under the care of Dr. John Owen at the Liverpool Royal Infirmary, and we are greatly indebted to him for permission to investigate and record it.

BRIEF HISTORY AND DESCRIPTION OF CASE

S. G., male, aged 52 years, married, had one child who died at 9 years of age from 'wasting'. His wife is healthy and has had no miscarriages. Family history negative. No previous serious illnesses. For 15 months

white corpuscles, 8,000 per c.mm.; differential count (per cent) on 400 white cells: polymorphs, 45.5; large lymphocytes, 5; small lymphocytes, 45.75; mononuclears, 1.25; eosinophils, 1.25; basophils, 0.5; myelocytes, 0.75. During this count three normoblasts and four megaloblasts were seen. An Arneth count (per cent) of the polymorphs gave: Class (1), 9.3; (2), 21.4; (3), 40.1; (4), 20.9; (5), 8.3; Arneth Index, 50.75. Blood film: Marked anisocytosis with megalocytic predominance, poikilocytosis and polychromatophilia. No punctate basophils seen. Normoblasts and megaloblasts present.

Wassermann reaction: Strongly positive. Fragility of red cells and coagulation time of blood (method of Dale and Laidlaw): Normal. Van den Bergh reaction: Negative direct; positive indirect reaction. Urine: Excess of urobilin and urobilinogen. Faeces: No parasites; no occult blood. Fractional gastric analysis: Complete achlorhydria with a very low total acidity (10 c.cm. N/10 HCl per cent); no blood nor bile.

Auto-agglutination was noticed during the routine blood examination. In diluting the blood for a cell count and in the preparation of blood films the phenomenon declared itself. That it was due neither to the apparatus nor to the solutions used was apparent from its repeated occurrence with new apparatus and fresh solutions. Moreover, on the same glass slide on which the auto-agglutination occurred with S. G.'s blood, blood from other patients remained non-agglutinated.

In order to study further this phenomenon of auto-agglutination, blood was withdrawn by venous puncture. A portion of this was allowed to clot and the serum collected; the remainder was citrated to prevent clotting, immediately centrifugalized, and the red cells carefully washed with warm saline (37°C.).

RESULTS

The following tables show the effects of varying dilutions of S. G.'s serum on his own cells and those of other groups at body and room temperatures. The cells and serum of pure members only of the four blood groups were used in this investigation.

The red cells of S. G. were not agglutinated by the serum of any normal blood group either at body or room temperature.

Tables showing effect of S. G.'s serum (diluted with normal saline) on the cells (2½ per cent suspension in normal saline) of the blood groups I, II, III, and IV.

Cells of group —	A					B				
	Dilution of S. G.'s serum					Dilution of S. G.'s serum				
	1/2	1/6	1/18	1/54	1/162	1/2	1/6	1/18	1/54	1/162
I	+++	++	++	+	+	+++	+++	+++	++	++
II	++	++	+	+	+	+++	+++	++	+	+
III	++	++	+	+	—	+++	++	++	+	—
IV	—	—	—	—	—	+++	+++	+++	++	+
S. G.	—	—	—	—	—	++	+	—	—	—

+ slight but definite agglutination;

++ marked but not complete agglutination;

+++ complete agglutination;

— no agglutination.

(A) at 37°C. and (B) at 12°C. (room temperature).

Certain facts which emerge from a study of the above are:—

1. The patient belongs to blood group IV, and his serum contains the iso-agglutinins for groups I, II, and III.

2. The power of auto-agglutination does not reside in the red corpuscles, since S. G.'s cells are not agglutinated by the serum of a normal member of any blood group.

3. Auto-agglutination occurs only at low temperature. S. G.'s blood be gradually

he has had paræsthesiæ of whole body, but especially of legs and feet, and gradually increasing weakness of legs and loss of energy.

On examination the typical features of pernicious anæmia associated with subacute combined sclerosis were present: lemon-yellow tint, marked pallor, little wasting, typical 'glossitic' tongue, marked weakness with loss of joint-muscle, and vibration sense in upper and lower limbs, increased deep reflexes and bilateral extensor toe response, etc.

The blood findings on admission were: Red corpuscles, 2,400,000 per c.mm.; hemoglobin, 44 per cent;

cooled auto-agglutination begins to appear at 22°C. to 26°C.; if after cooling the same set of tubes be gradually warmed, auto-agglutination remains in some degree until 32°C. to 34°C. is reached, thus demonstrating the reversibility of the reaction.

4. (a) The agglutinating power of S. G.'s serum is for all groups greater in the cold than at body temperature. (b) The agglutinating power in the cold of S. G.'s serum is greater for cells from normal members of his own group (IV) than for his own cells.

Additional facts we have determined are:—

5. The auto-agglutinin of S. G.'s serum agglutinates the cells of—

- (a) Rabbit (dilution of serum 1/486+).
- (b) Guinea-pig (dilution of serum 1/162+).
- (c) Sheep (dilution of serum 1/18+).
- (d) Goat (dilution of serum 1/18+).

Other workers have shown, and our observations confirm, that this agglutination is distinct from that due to hetero-agglutinins normally present in serum.

6. Auto-agglutination is associated with the removal from the serum by the red cells of the auto-agglutinin*; for if S. G.'s serum be mixed with a suspension of his cells in the cold, allowed to stand and the mixture be then centrifuged, the supernatant fluid does not contain the auto-agglutinin, though the iso-agglutinins for groups I, II, and III can be demonstrated.

7. There is no evidence of auto-phagocytosis in S. G.'s blood (Prof. E. E. Glynn), nor of any auto-hæmolysis.

DISCUSSION

Clough and Richter, in their paper 'A Study of an Auto-agglutinin occurring in a Human Serum', have recorded fully a case of chronic mitral endocarditis with broncho-pneumonia which showed this phenomenon. They make no reference, however, to its occurrence in trypanosomiasis, clinical and experimental, probably the commonest condition by far with which auto-agglutination is associated, and they appear to have overlooked a paper by Warrington Yorke, in which are recorded fully and accurately the effect of temperature on auto-agglutination, the adsorption of agglutinin by the red cells, the reversibility of the process, and the effect of the agglutinin on the cells of other animals.

Clinically, auto-agglutination has been observed in the following conditions:—

1. Trypanosomiasis (Kanthack, Durham, and Blandford; Christy; Dutton and Todd; Martin, Leboeuf, and Roubaud; Yorke, etc.).
2. Cirrhosis of the liver (Reitmann; Klein).
3. Relapsing fever (Todd; experimentally in rats by Nattan-Larrier).
4. Syphilis (Dudgeon; Todd).
5. Long-standing epilepsy (Dudgeon).
6. Certain forms of icterus due to hæmolysis (Martin and Darre).
7. Broncho-pneumonia with chronic mitral endocarditis (Clough and Richter).
8. Marked secondary anaemia due to hæmorrhage from hæmorrhoids; and heart disease (Kliger).
9. Pernicious anaemia with subacute combined sclerosis and a positive Wassermann reaction (Cohen and Jones).

Apart from trypanosomiasis, in which auto-agglutination is said to occur in the large majority of cases, the literature contains references to only one or two cases of the above conditions in which auto-agglutination was found, and some of these are doubtful. One of us (H. C.) has examined the bloods from 300 individuals since the occurrence of our case, but not one showed the marked auto-agglutination found in S. G. Those examined included 11 cases of pernicious anaemia—6 with subacute combined sclerosis, 4 cases of cirrhosis and syphilis of the liver, 3 cases of hæmolytic icterus, and many severe secondary anaemias. Forty of these cases were associated with a positive Wassermann

reaction. We must conclude that auto-agglutination is thus a rare phenomenon, not constantly associated with any pathological state.

The daughter of Clough and Richter's patient showed auto-agglutination in her blood. They suggested that since it was present in both mother and daughter, the phenomenon is an hereditary peculiarity. The only living relations of our patient, an elder brother and his son, showed no auto-agglutination, both of them being normal members of group IV. That auto-agglutination can be acquired is shown not only by its very frequent occurrence in trypanosomiasis, but also by the experimental work of Rous and Robertson, who were able to induce auto-agglutination in rabbits by the repeated withdrawal of moderate quantities of blood.

In view of this experimental work we examined the blood of the following five donors:—

1. R. H. P. who between June 1921 and August 1924, had on each of six occasions given one pint of blood.
2. T. H. who between February 1922 and July 1923 had on seven occasions given one pint of blood.
3. W. L. who had in January 1921, also in May and June 1924, given one pint of blood.
4. W. H. who had in March 1923 given one pint of blood.
5. W. H. E. who during the past three years had almost weekly given 20 to 50 c.cm. of blood for experimental purposes, and in July gave one pint of blood as a donor.

All these cases proved negative, no trace of auto-agglutination being found.

Of the mechanism of production and the chemistry of the auto-agglutinin we are ignorant. Its occurrence in anaemias has led to the suggestion that the auto-agglutinin results from the inoculation of the organism with the products of disintegration of its own erythrocytes, but this seems negatived not only by the very rare occurrence of auto-agglutination in anæmic states but also by the impossibility of experimentally producing an auto-agglutinin in the blood of an animal by injection of its own red cells.

Another suggestion, that the auto-agglutinin develops in direct response to the stimulus of a pathogenic agent, is of interest in view of the similar protozoal aetiology of trypanosomiasis, relapsing fever and syphilis, conditions in which auto-agglutination has been clinically described. The increased acidity of the blood said by Nicrenstein to occur in trypanosomiasis has been suggested by Breinl and himself to be the cause of auto-agglutination in that disease.

Can auto-agglutination be looked on as part of the body's resistance to disease? Since the phenomenon does not occur at body temperature, any effect it will exert is probably at the surface. Its only value here would seem the diminution of bleeding from small wounds by plugging the vessels with agglutinated cells, and thus preventing the further impoverishment of the blood volume in severe anaemias.

Practically recognition of the phenomenon of auto-agglutination may account for some of those cases, which, when grouped by the glass-slide method with the sera of groups II and III, are said to show a change in group from IV to I, when typed at a later date. Thus, had S. G. been tested by this method, he would have been called group I, because his own serum would agglutinate his erythrocytes even when mixed with serum of group II, or III. The consequence of transfusing a patient with blood from a donor who shows auto-agglutination is not likely to have serious effects, provided the blood be slowly injected, since the body temperature prevents the occurrence of the auto-agglutination.

Whilst, therefore, the practical advantages which result from a study of auto-agglutination in human blood seem small, its scientific interest is considerable.

Note.—Since the above paper was written a further case of auto-agglutination in pneumonia is recorded by E. Claveaux and Pérez Sánchez. The phenomenon was noticed during convalescence from the disease. The

*? Adsorption of agglutinin by the cells; this is supported by the reversibility of the process—i.e. on warming, the auto-agglutinin is liberated.

nente attack had been treated with injections of patient's own blood.

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Yellow Fever in the Anglo-Egyptian Sudan: The Differential Diagnosis of Yellow Fever

By G. M. FINDLAY

R. KIRK

and

D. J. LEWIS

(Abstracted from the *Annals of Tropical Medicine and Parasitology*, Vol. XXXV, 31st December, 1941, p. 149)

THE difficulty in diagnosing yellow fever in the field by clinical means is well illustrated by the present account of two epidemics, not of yellow fever, but misguidedly with jaundice and black vomit, occurring during 1940 in the Tagoi Hills and in and around El Oheid, at the same time as yellow fever was present in other parts of the Province of Kordofan.

The clinical symptoms of the two epidemics are based on 33 cases, three of which were fatal. The following is a summary of the principal symptoms of these 33 patients studied in detail :—

Fever ..	33	Epistaxis ..	11
Headache ..	33	Vomiting ..	11
Jaundice early 10	25	Black vomit ..	3
late 15		Hæmorrhage from bowels ..	4
Backache ..	20	Residual enlargement of liver ..	4
Pains in limbs ..	18	Epigastric pains ..	2
Diarrhoea ..	12		

The urine contained albumin in addition to bile. Differential blood counts showed polymorphonuclear leucocytosis. No malaria parasites were found, but in two patients whose blood was examined at the height of the fever, *sporochytes* were present.

Careful experimental investigations excluded the possibility of yellow fever and after a discussion of all the possibilities the authors bring forward evidence to show that relapsing fever and infective hepatitis, in addition to yellow fever, were present in epidemic form in Kordofan Province during 1940.

In view of the various diseases in the tropics that may produce jaundice accompanied by black vomit, it is obvious that laboratory procedures are essential

for the rapid and accurate diagnosis of yellow fever, and in countries where it exists, or may spread, laboratories should be equipped to carry out the isolation of the virus by inoculation into susceptible animals, the histological investigation of liver sections from fatal cases, and mouse protection tests on the blood.

(Abstract adapted from *Tropical Diseases Bulletin*, 39, 457, July 1942.)

Malarial Hæmagglutination

(From the *Journal of the American Medical Association*, Vol. CXXI, 23rd January, 1943, p. 263)

AN interesting contribution to the pathology of malaria is contained in a study of intravascular hæmagglutination in birds infected with *Plasmodium cathemerium*, currently reported by Lack of the University of Tennessee. Using the Knibely quartz rod microilluminator, the investigator studied the histopathology of the circulation in the wing web of normal and experimentally infected canaries. A drop of liquid petrolatum placed on the epithelium facilitated visualization at a magnification of 96 diameters. All experimentally infected birds developed parasites in the blood stream with counts up to 67 per cent, from which all but one bird died. As the parasite count began to rise there was an initial loss of 'streamlining' in the peripheral circulations accompanied by transient sticking of leucocytes to the endothelial lining of the venules plus evidence of plasma leakage. As the count increased the white cells became adherent to the endothelium in ever increasing numbers, accompanied by the formation of sticky clumps of red cells, which retarded the rate of blood flow in many areas. In the subsequent twenty-four to forty-eight hours came progressive intravascular clumping. The clumps were now fairly firm, could withstand intravascular stress and occasionally appeared in the arterioles. Plasma viscosity was apparently increased. The clumps were originally formed only by parasitized cells but later included both infected and normal erythrocytes. The final stage was a 'paste-like' blood flow followed by death of the bird within a few hours. Intravascular agglutination had previously been described in experimental malarial monkeys by Knibely and his co-workers of the University of Chicago. The phenomenon presumably occurs in man.

Infective Hepatitis: The History of an Outbreak in the Lavant Valley

By J. L. NEWMAN

(Abstracted from the *British Medical Journal*, Vol. I, 17th January, 1942, p. 61)

THIS outbreak consisted of 33 cases in which there were two main streams of infection which the author follows from family to family. Clinically the disease ran true to type, but some cases simulated Weil's disease and some acute conditions of the lungs, abdomen or central nervous system. From a study of the cases the view is expressed that the patient becomes infective very early in the disease and that he has ceased to be a danger to others about a week after the onset of symptoms. On the controversial point of the incubation period the author is of the opinion that it is a long one, and in one instance he was able to establish this as from 29 to 31 days. Infection is from case to case but the author is not in accord with the droplet theory and prefers the admittedly unsatisfactory explanation of air-borne infection with the proviso that receptivity to infection must be phasic or intermittent. Tabulation of the attack rates at the various age groups revealed that the older members of the community were as susceptible as the younger, but the numbers are small. With regard to control it is important to remember that the condition is infectious and once a case has occurred the medical officer should be on the lookout for secondary cases. Contacts should be warned to report at once if in doubt

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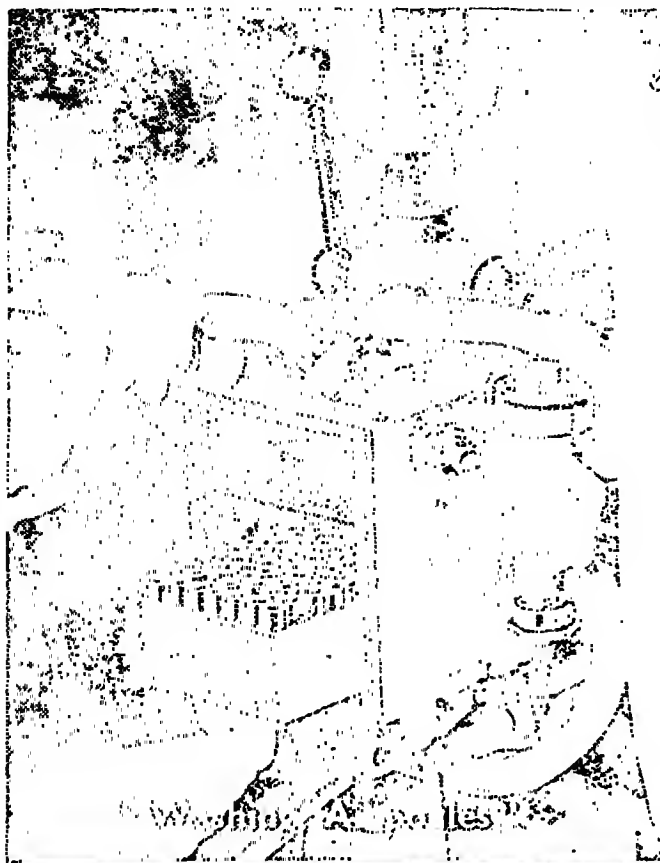


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a month gastric symptoms appear so that these can be dealt with.

(Abstract adapted from *Bulletin of Hygiene*, 17, 407, June 1942.)

Sulphamethazine: Clinical Trial of a New Sulphonamide

By D. W. MACARTNEY

G. S. SMITH

R. W. LUXTON

W. A. RAMSAY

and

J. GOLDMAN

(Abstracted from the *Lancet*, Vol. I, 30th May, 1942, p. 639)

SULPHAPYRIDINE and sulphathiazole have been extensively used in the treatment of pneumococcal infections. More recently sulphadiazine has also been employed for the same purpose. These compounds may produce various toxic manifestations such as nausea and vomiting and renal damage due to the formation of crystals in the urinary tract.

In the summer of 1941 the attention of the present authors was drawn by Drs. Martin and Rose of the research laboratories of Imperial Chemical (Pharmaceuticals) Ltd. to a near relation to sulphadiazine, namely, 2-(4-aminobenzene-sulphonylamino) 4:6-dimethylpyrimidine—to which the name *sulphamethazine* has been given. Laboratory examination of this substance had shown that it had the same order of therapeutic potency as the other sulphonamides, but that the relatively high water solubility of the drug and its acetyl derivative suggested that it would be less likely to cause renal injury.

Sulphamethazine forms pale yellow crystals with a melting point of approximately 83°C. In the present investigations it has been employed in this form and also as a 33 per cent weight/volume solution of the sodium salt (pH 9.6).

This paper is mainly concerned with the results of a clinical trial of sulphamethazine in the treatment of lobar pneumonia, a note being made of its use in a few cases of meningococcal meningitis and of gonorrhoea.

Three diagnostic criteria were strictly adopted for each of the cases of pneumococcal lobar pneumonia included in the survey:

- (1) A history of pain in the chest and of rigor at the onset of the illness.
- (2) Clinical and radiological evidence of pneumonic consolidation.
- (3) The isolation and typing of a pneumococcus from the sputum.

As soon as the diagnosis was made, and before treatment was begun, blood was taken for culture and this procedure was repeated in 24 hours if pyrexia persisted. In many of the cases the blood levels of the drug and the amount excreted in the urine were estimated.

DOSAGE, BLOOD LEVELS AND EXCRETION

As the drug appeared to be well tolerated pneumonia cases were given an initial dose of 4 g. followed in most cases by 2 g. every six hours. In critically ill patients, where the blood level was less than 4 mg. per 100 c.cm., 2 g. was given every four hours until there was obvious clinical improvement. The sodium salt was supplied in ampoules of 3 c.cm. containing 1 g. for intravenous use and was usually diluted with distilled water to 8 c.cm. No reactions were observed after these injections.

A blood concentration of the drug of approximately 8 mg. per 100 c.cm. was usually reached in from one to three hours after the administration of 4 g. by mouth. On the standard dosage of 4 g. followed by 2 g. every six hours the blood level was extremely

variable as between individual cases, ranging from 2 to 13.5 mg. per 100 c.cm., but the average level was approximately 6 mg. per 100 c.cm.

The urinary excretion over 24-hour periods was usually found to be between 25 per cent and 50 per cent of the amount given by mouth.

In four of the six cases of cerebrospinal meningitis where the blood level was estimated at the same time as that of the cerebrospinal fluid, the concentration of the drug in the latter was from 50 per cent to 80 per cent of that in the blood.

No abnormal blood pigments were found.

RESULTS OF CLINICAL TRIAL

Seventy-three cases of pneumococcal lobar pneumonia were treated with sulphamethazine. The series comprised 55 males and 18 females. The total mortality was 5 out of 73 cases which is similar to that which occurred in a larger series of cases treated with sulphapyridine in 1940 by Don, Luxton, Donald, Ramsay, Smith and Adderley (1940). Of the fatal cases, 4 were bacteremic, 3 giving a pneumococcus type 1 and one a type 2, while 10 other bacteremic cases recovered.

Clinical improvement was generally noticed within 24 hours of the commencement of treatment and was similar to that following sulphapyridine therapy. The patients however did not complain of the severe mental and physical depression which often accompanies sulphapyridine treatment. Cyanosis was not observed. Nausea and vomiting occurred in only 5 out of the 73 cases and was not severe. Only 2 patients developed complications. A woman aged 52 with a positive blood culture died from pneumococcal meningitis and endocarditis. The second case was a man who developed jaundice three days after the cessation of treatment.

Six cases of meningococcal meningitis were treated and all recovered. Two of them were admitted in an unconscious state and received the drug intravenously as well as intramuscularly.

Nine cases of gonorrhoea were treated in hospital with 2 g. every 4 hours for five days followed by an interval of 2 days and a repetition of the course. All signs of the disease disappeared and the various tests were negative.

TOXICITY

Nausea and vomiting were very much less frequent than with sulphapyridine and when they did occur they were transient and did not make it necessary to suspend treatment. Cyanosis did not occur. Two cases developed rashes.

There was no evidence of renal damage. All urines were repeatedly examined for crystals. There was no evidence of agranulocytosis. Drug fever occurred in only one of the gonorrhoea cases.

CONCLUSIONS

The authors believe that sulphamethazine is as effective as sulphapyridine in the treatment of lobar pneumonia. Owing to its high solubility it is more rapidly absorbed than sulphapyridine and it is therefore possible to reach a high blood level more rapidly.

Both sulphapyridine and sulphadiazine are liable to cause renal damage, possibly because of the mechanical action of the crystals of the drugs which may be excreted in the urine. Sulphamethazine and its acetyl derivative are so soluble that renal damage from crystal formation should never occur.

The results in the small number of cases of meningococcal meningitis and gonorrhoea suggest that the preparation is likely to be of value also in these infections.

Owing to the extreme variability in the absorption and excretion of the sulphonamides in different individuals and to the necessity for maintaining a high blood level of the drug in serious cases it seems advisable to estimate the blood concentration in all cases where clinical improvement is delayed. If necessary the sodium salt should be given intravenously.

Bismuth in Syphilis

(From the *Lancet*, Vol. II, 10th December, 1942, p. 730)

ALTHOUGH undoubtedly rapid in antisyphilitic action arsphenamine soon proved its inability to deal alone with syphilis infection in its entirety. In the early years this inability was compensated by the retention of mercury as a supporting agent, but from 1921 onwards that veteran was gradually superseded by bismuth. For many years now it has been traditional in European circles to treat the early lesions of syphilis with both these remedies, either at the same sitting or within the same week, and since this combined therapy seemed satisfactory it was natural that efforts were made to produce a stable chemical union of these two agents which would combine not only their structure but also their antisyphilitic effect. Such a combination of bismuth with a pentavalent arsenical was launched in 1925 by Levaditi under the name of 'Bistovol' (bismuth stovarsol), which contained 15 per cent of arsenic and 41 per cent of bismuth. Some degree of antisyphilitic effect was reported for this compound but its use never became widespread and evidently the union had failed to achieve the desired summation of the efficacy of the two components. In the meantime there have been trials of other combinations, such as bismuth arsanilate and bismuth tryparsamide, but reports on their success or otherwise have been scanty.

Another of these compounds, 'Bismarsen', synthesized by Raiziss in 1925, has been used over a period of fourteen years by Beerman, Shaffer and Livingood of Philadelphia. This preparation, defined as bismuth arsphenamine sulphonate, containing 13 per cent of arsenic and 24 per cent of bismuth, is a welding of the bismuth element into a trivalent arsenical—the arsphenamine base—in contrast to the inclusion of the less active pentavalent arsenical radicle exhibited in bistovol. It does not seem to be the hoped for fully effective combination, for Beerman and his co-workers found it appreciably less successful than bismuth and arsphenamine administered separately. The healing effect on early syphilitic lesions was good but slow and the relapse rate about 12 per cent. Systemic reactions were met with after only 0.5 per cent of injections, and the compound appears to have been well tolerated by sufferers from late syphilitic affections, particularly cardiovascular lesions, which showed some encouraging improvement. Among the 823 patients there were 5 examples of arsphenamine dermatitis and 5 of purpura hæmorrhagica. There were no deaths, and no examples of hepatitis or jaundice, though this complication has been reported occasionally by others using bismarsen. The long-term results are of special interest. Of 71 patients treated for early syphilis and observed for periods ranging from six months to fourteen years, serological relapse occurred alone in 4 and in conjunction with the reappearance of infectious surface lesions

in 4 others. One or more examinations of the cerebrospinal fluid were made during the period of observation in 48 of these 71, and only 6 showed any abnormality; about half of the patients with fixations showed a later reversal to a healing of the tertiary osseous and cutaneous lesions in middle-aged and elderly patients takes place more slowly, it seems that bismarsen may be used with advantage in these patients especially when they do not tolerate other organic arsenical compounds well.

Postarsphenamine jaundice, under the title of 'Salvarsan' jaundice, was a formidable interrupter of treatment and a cause of ill health and some deaths during the last war, and there has lately been a recurrence of the unsatisfying discussions on the rôle played by suspected factors other than arsphenamine in its production. The old ground of alcohol, diet, vitamins, intercurrent infection and so on has been explored again without bringing to light any very illuminating facts, but although instances of jaundice following bismuth treatment alone are occasionally encountered the possibility of bismuth being a factor seems to have been neglected. Kulchar and Reynolds report that of the 1,032 male prisoners in the United States prison at San Quentin receiving treatment for syphilis between 1936 and 1942, 144 (13.9 per cent) became jaundiced, and in 121 (10.3 per cent) of these jaundice appeared while bismuth was being given. The treatment system consisted of neoarsphenamine or 'Mapharsen' in courses of ten weekly injections in alternation with courses of twenty weekly injections of sodium iodobismuthite. There was no epidemic of catarrhal jaundice among the prisoners during the period of this study and the endemic rate was low—0.1 per cent in 1941. Among the 121 cases of jaundice during bismuth treatment, 4 became jaundiced during the first course of bismuth, and previous arsenical therapy could be excluded. The remaining 117 received arsenicals in some form before the course of bismuth during which the hepatitis occurred. Jaundice began within four weeks of the last injection of an arsenical in 34 cases and in these the arsenic is considered as a possible factor. Jaundice was not evident until the fourth to the eighth week of bismuth therapy in 83 cases and in the ninth week or later in 56 cases. It was thought that the time intervening since the last injection of an arsenical in these cases made it unlikely that the jaundice was entirely due to previous arsenical therapy. Many syphilologists, however, would not accept this short time limit as permitting the exclusion of arsenic as a possible factor, for examples of postarsphenamine jaundice may be met with up to four or five months after the last arsenical injection. Although the evidence presented by Kulchar and Reynolds for ascribing a major rôle to bismuth in these cases is not unequivocal, their report serves as a reminder that bismuth puts an additional load on the liver, and might, like arsenic, prepare the ground for virus infection.

Reviews

THE OFFICIAL HISTORY OF THE AUSTRALIAN ARMY MEDICAL SERVICES IN THE WAR 1914-18. VOLUME III. SPECIAL PROBLEMS AND SERVICES.—By Colonel A. G. Butler, D.S.O., V.D., B.A., M.B., Ch.B. (Camb.). 1943. Published by Australian War Memorial, Canberra. Pp. xx plus 1103 with 85 illustrations, graphs and diagrams. Price, 21s.

This book has been received from the Australian War Memorial, Canberra. The notice accompanying this book reads as follows:—

This third volume completes the official Australian medical history of the war 1914-18, and with it the series of Australian official histories of that war. In

the two previous volumes the study made of medical problems and events was deliberately and exactly based on their military history. The present volume approaches the subject with a wider perspective and more objective outlook. The perspective contains, in some degree, the history of mankind as well as of that war; the outlook is that which affirms *Homo sum, humani nihil a me alienum puto*. The First World War is seen as an episode of continuing significance and interest for the human race; and for that reason, even more than for its direct lessons, as worthy of philosophic and social, as well as medical and military study.

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The Principles and Practice of Tropical Medicine

By **L. EVERARD NAPIER, C.I.E., F.R.C.P.**

DIRECTOR AND PROFESSOR OF TROPICAL MEDICINE, CALCUTTA SCHOOL
OF TROPICAL MEDICINE, SUPERINTENDENT AND SENIOR PHYSICIAN,
CARMICHAEL HOSPITAL FOR TROPICAL DISEASES. CALCUTTA

CONTENTS OF PART I

PREFACE	Tsutsugamushi
INTRODUCTION	"Q" fever
MEASURES FOR MITIGATING THE EFFECTS OF TROPICAL CLIMATE	Typhus fever in India
DISEASES DUE TO THE DIRECT EFFECTS OF TROPICAL CLIMATE	OROYA FEVER, OR BARTONELLOSIS
MALARIA	YELLOW FEVER
Blackwater fever	RIFT VALLEY FEVER
LEISHMANIASIS	DENGUE SAND-FLY GROUP
Kala-azar	Dengue
Oriental sore	Sand-fly fever
South American mucro-cutaneous leishmaniasis	PLAGUE
TRYPANOSOMIASIS	TULAREMIA
Sleeping sickness, or African trypanosomiasis	THE UNDULANT FEVERS
Chagas's disease, or South American trypanoso- miasis	Malta fever
THE RELAPSING FEVERS	Abortus fever
Louse-borne relapsing fever	MELIOIDOSIS
Tick-borne relapsing fever	THE INTESTINAL FLUXES
RAT-BITE FEVER	Cholera
LEPTOSPIROSIS	Bacillary dysentery
Weill's disease, or infective jaundice	Flies
Seven-day fever of Japan	Amœbic dysentery
THE TYPHUS FEVERS	Amœbic hepatitis and liver abscess
The typhus fevers	Other protozoal and metazoal dysenteries and diarrhœas
Classical, epidemic, or louse-borne typhus	Chronic post-dysenteric ulcerative colitis
Trench fever	Sprue
Endemic, or murine, typhus	Para-sprue
Rocky Mountain spotted fever	Hill diarrhœa
	LEPROSY

The Publication of this book is very timely. Normally there is a considerable demand in India for books on tropical medicine and this demand has been greatly increased by the large number of medical men coming to India from other countries. Moreover, the standard textbooks on tropical medicine have become difficult or impossible to obtain in India.

The book, however, is not merely a substitute for standard works but is an important contribution to the literature on tropical medicine. It is based very largely on the experience of Dr. Napier as Professor of Tropical Medicine in the Calcutta School of Tropical Medicine. Dr. Napier is of course known throughout the world for his work in tropical medicine and moreover he has had much help from the experienced colleagues at the Calcutta School of Tropical Medicine, and the result is a book on tropical medicine of real practical value written from first-hand experience.

The contents page of Part I is given above and it will be seen that this volume covers most of the important tropical diseases. The chapter on leprosy occupying 42 pages is by Dr. John Lowe and is entirely a new presentation of the subject.

Being an entirely new book this work will be found to be more up-to-date than other similar books. A feature of the book is the attention paid to the subject of epidemiology and to all matters connected with it. The author stresses the basic principles of tropical medicine and relates them to the known facts and to the practice of tropical medicine.

The author could not complete the book before he left India and it was decided that, to meet the immediate demand, it was advisable to publish the book in two parts. The first part, dealing with nearly all the major tropical diseases in 522 pages, is practically a complete work in itself. The second part which should be ready in a very few months will be about half the size of the first part and will include chapters on yaws, tropical ulcerative conditions, helminthic infections, diet and dietetic diseases, anemia in the tropics, snakes and snake-bite, etc.

At present the first part is being issued in a good but temporary binding of cloth-covered board. Later, when the second part is ready, the book will be available complete in one volume.

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of the accessory services of succour—Dental, Pharmaceutical, Nursing, and Massage (physiotherapy); together with a survey, necessarily cursory, of the medical experience of the Royal Australian Navy and the newly created 'Australian Flying Corps'. The remainder of the volume is occupied with a study of the involvements of the army medical service and the civil medical profession in the problems of the invalid and the war damaged soldier. The terrible problems of the aftermath are approached from a strictly medical angle; and its events and problems are examined from a national as well as from the service standpoint.

The epilogue asks *quo vadis*, and endeavours to answer this question. It is approached through the threefold allegiance of the medical service—to the Army, to the Nation, and to Humanity. Its purpose includes a brief appreciation of the place in modern warfare of the International Red Cross, as seen in the work of the Australian Branch of the British Red Cross Society; and of the relations between the Medical Service and the Army Chaplain Department and the Y. M. C. A.

YOU AND YOUR COMRADES: HOME GUARD MEDICAL MANUAL. (FRONT LINE TREATMENT OF WOUNDS).—By The Medical Officer to Midlothian Battalion Home Guard, 1943. E. and S. Livingstone, Edinburgh. Pp. 31, with 3 figures. Price, 4d.; postage 1d.

THIS little manual measuring 2½ inches by 4 inches and costing 4d. was especially prepared for rapid instruction in First Aid of the Home Guard in Great Britain. The introduction contains the following sentence:—'These instructions are for the use of all ranks in the Home Guard: they are in non-technical language and are severely practical. They are limited to procedures which have to be carried out during battle.'

This little manual appears to be excellent. Most of the jargon of the First Aid is omitted and this process might have been carried even further. Haemorrhage might have been called bleeding all through and not only in a few places. Fractures might have been 'fixed' instead of immobilized. In general the English is simple and clear, though there are occasional lapses. Men are told 'to memorize the location of shelters' instead of to remember where the shelters are. It is good to see the word 'crepitation' avoided and the expression 'a crunching feeling' used.

A booklet along these lines might be much more useful in India than the usual First Aid manuals.

J. L.

BROMPTON HOSPITAL REPORTS: A COLLECTION OF PAPERS RECENTLY PUBLISHED FROM THE HOSPITAL. VOLUME X, 1941.—Published by the Research Department of the Hospital. Printed in England by Gale and Polden Limited, Aldershot. Pp. 127. Illustrated. Price, 5s. (Further copies can be obtained from the Secretary, The Hospital for Consumption, Brompton, London, S.W.3. Price, 5s. 7d., post free)

THIS volume contains a batch of ten papers recently published by members of the staff of the Brompton Hospital. The first three deal with surgery of the chest, the subjects treated being drainage of the pleura, closed wounds of the chest, and traumatic hæmothorax. In the next article 'The ætiology of sub-acute pulmonary infections', Maurice Davidson and Philip Ellman give an interesting account of five cases in which the radiological appearances and clinical findings, the former more than the latter, were suggestive of pulmonary tuberculosis, but the sputum was persistently negative and eventually there was resolution, the physical signs and the x-ray opacity clearing up. The possible causes are discussed, but after considering the available data, the authors come to the conclusion that they were cases of atypical pulmonary tuberculosis. Then there are three articles on bronchial growths—adenoma, carcinoma and chondroma. Of adenoma

twenty-two examples are described which have been seen at the Brompton Hospital. The condition is often confused with pulmonary tuberculosis and bronchial carcinoma, and the author, A. F. Foster-Carter, stresses on the importance of its early recognition by bronchoscopy and cites a few instances to illustrate how easily a bronchial growth may be overlooked. Thus one patient with cough and hæmoptysis was at first thought to have a lung abscess and later phthisis, for which he was treated over 11 years, mostly in sanatoria, before the bronchial tumour was discovered. F. C. Ormerod describes the technique of treatment of bronchial carcinoma by the application of radon, and gives an account of five patients thus treated who are alive and well two years and more after their original treatment. There are also papers on chronic empyema and erythema nodosum and the volume ends with an article 'The persistence of lipiodol in the lungs following bronchography'. There are many illustrations and most of the papers are of practical interest. The reviewer who happened, by the way, to be a clinical assistant in the Brompton Hospital at one time, has pleasure in recommending it to all those who are interested in injuries and diseases of the chest.

R. N. C.

NUTRITIONAL DEFICIENCIES, DIAGNOSIS AND TREATMENT.—By John B. Youmans, A.B., M.S., M.D. Assisted by E. White Patton, M.D. 1941. J. B. Lippincott Company, Philadelphia and London. Pp. xii plus 385, with 16 illustrations. Price, 30s.

THE literature on vitamins has grown so vast and bewildering and there are so many contrary views that it is difficult for practitioners to assess their true value and keep abreast of genuine new developments. This no doubt largely accounts for much of the present-day 'shot-gun' practice in vitamin therapy. We therefore welcome this book as presenting a clear and reasonable account of the essential food factors and their deficiencies. The vitamins necessarily occupy a large portion of this book; it also includes chapters on proteins, iron, iodine and calcium deficiencies. The ætiology, pathogenesis, diagnosis, etc., are clearly described and emphasis has been laid on the preventive aspects of treatment. The author dwells on the importance of early recognition of mild or sub-clinical deficiencies, but points out the difficulties of diagnosis in such cases. In the appendix is given a tabular summary of the vitamins, their principal sources and details of the technique of the various laboratory tests. It is a well-balanced book, keeping mainly to established facts and avoiding exaggerated claims, and will help practitioners towards understanding and management of nutritional deficiencies in practice.

R. N. C.

A SYNOPSIS OF REGIONAL ANATOMY.—By T. B. Johnston, M.D. Fifth Edition. 1943. J. and A. Churchill Limited, London. Pp. viii plus 424, with 17 illustrations. Price, 16s.

THE difficulty of remembering anatomical structure lies in the fact that in textbooks the essentials are mixed up with an overwhelming mass of detail which has been found from experience to be unnecessary and of little practical utility. For this reason the author endeavoured to condense topographical anatomy to the requirements of clinical studies in medicine and surgery, eliminating the mass of unimportant detail, and producing this book which was first published about two decades ago.

That the purpose of the author has been fully achieved will be seen from the fact that succeeding editions have become necessary in progressively shorter intervals—a sure testimony of increasing appreciation of his effort and greater usefulness of this production.

The book is meant mainly, as the author has indicated, for purposes of revision and should therefore not be used before the student has acquired first-hand knowledge from dissection and is thus ready for

revision. As we also share the author's apprehension that this advice, albeit very sound, may be disregarded, we feel it necessary to stress that one would be sadly disappointed to take it as a substitute for a textbook; and that to make its perusal profitable, the student must use it at the appropriate time and take it as a supplement to make his heavy study of textbooks an easier task.

By skilful excision and condensation, the author has not only been able to effect a reduction of 37 pages of the actual text without affecting its usefulness, but has actually made an improvement on the previous issues by including 'additional references to the functional aspects of the subject' which is sure to make the reading more interesting and useful. We have no doubt that the present edition will be more widely accepted now than ever before, as the need of such books is clearly manifest when the course of preclinical studies is engaging greater attention owing to changes in the curriculum. The book can be recommended without any reservation to all who are on the look out for a shorter but reliable text for revisionary purposes.

S. C. S.

THE TREATMENT OF SHOCK.—By R. W. RAVEN, F.R.C.S. (Major, R.A.M.C.). 1942. Oxford University Press, London. Humphrey Milford. Pp. xii plus 96. Illustrated. Price, 5s. Obtainable from Oxford University Press, Bombay and Calcutta

THE appearance of this short manual is timely. In probably no sphere of medicine just now is education of the profession more needed than in the treatment of shock. The author has succeeded in presenting the subject concisely but has unfortunately allowed quite a number of errors to enter.

The classification of shock is satisfactorily dealt with. Describing the clinical picture he states that 'there is apathy, stupor, delirium and unconsciousness'. This is uncommon. Undue stress is placed on local plasma loss and hæmoconcentration in the chapter on the pathology. In most cases hæmorrhage has occurred and hæmoconcentration is then not found.

The fluid dosage recommended in dehydration is inadequate. Moderation in warming shocked patients is advised—a good warning.

Concluding chapters deal in detail with oxygen administration, transfusion apparatus, anaesthesia and surgical operations in shock. The methods of preparing and drying plasma given most prominence were better omitted.

It is a useful little book which should be read critically and in conjunction with recent papers on the subject.

J. R. H.

Correspondence

A PLEA FOR A MORE COMPREHENSIVE OUTLOOK ON THE HUMAN BODY

SIR,—Colonel Cox, in his article with the above title, which was published in your June issue of the *Gazette*, has spoilt a very interesting thesis by some unwarranted and sometimes actually wrong generalizations. Thus in his experience with herbivorous humans he has seen far more suffering and sickness than among carnivorous people. Colonel McCarrison's experience is however otherwise and his notes on the subject will bear repetition. Referring to the people of Hunza he says 'My own experience provides an example of a race unsurpassed in perfection of physique and in freedom from disease in general whose sole food consists to this day of grains, vegetables and fruits with a certain amount of milk and butter and goat's meat only on feast days

(which means once in 2 or 3 months). They have in addition to grains, wheat, barley and maize an abundant crop of apricots. These they dry in the sun and use very largely in their food. Among these people the span of life is extraordinarily long and such service as I was able to render them during some 7 years spent in their midst was confined chiefly to accidental injuries'.

Considering their primitive conservancy arrangements and primitive housing in the rigorous Himalayan climate he says 'It is obvious that enforced restriction to the unsophisticated foodstuffs of nature is compatible with long life and continued vigour and perfect physique'. The Sikhs of the Punjab in the villages even up to 25 years ago did not use any meat for months at a stretch and yet their diet of milk and dal and wheat gave the Indian Army some of its finest recruits. The U. P. Brahmans and the Gour Brahmans, who owing to unfortunate political influences have not been able to emulate this time their recruiting records of the last war, have been described by many observers including Kim in the *Statesman* as the tallest and finest soldiers in the Indian Army. Yet they are vegetarians from time immemorial, i.e. for at least 2,000 years. Similarly the Brahmans and Chattris of West Behar who till lately formed the bulk of the Calcutta Police force are all vegetarians to a man and yet they are as fine a body of men as seen anywhere in the world. With these extraordinarily healthy and fine specimens of Hindus reared on a wholly herbivorous diet to describe vegetarians as pot-bellied hyperglycemics with hepatic and pancreatic failure or both at 40, with a high death and sickness rate on the basis of his experience of a ragi or cholam eating population, seems wholly unwarranted.

The Chinese soldiers, who may well be called the discovery of this war as giant killers, have been lately allowed by their Generalissimo an allowance of 26½ oz. of rice per diem and nothing else is mentioned in the order but presumably they take meat when they get it which is not always. Even then Colonel Cox's theory would make these soldiers on an enormous rice diet, miserable pot-bellied fatulent specimens of humanity, which assuredly they are not.

Colonel Cox has used the word herbivorous to mean all who are not meat eaters. The difficulties and disabilities which are associated with a cellulose predominating milkless diet he apparently associates with all meatless diet even though it be wheat, legume and milk. This is certainly far from correct.

Colonel Cox's dictum that milk is not an article of food and may serve only to quench thirst at the cost of much flatulence and discomfort is to say the least an amazing statement. The adult stomach may lack rennin but one can only ask Colonel Cox to reproduce normal conditions, put a pint of milk in a jar with adequate amounts of a 2 per cent hydrochloric acid solution and pepsin and watch the result.

Any one with any clinical experience knows that in the matter of milk each man is a law unto himself. There are some people who cannot stand milk at all and there are adults who thrive on it. A stomach educated to take a milk diet from the day the child is weaned will generally continue to stand milk and like it, while children who have not been continuing the milk habit will sometimes find themselves unable to digest milk when they grow up.

Colonel Cox is surely aware that in America, specially in the Eastern Seaboard States, it is the rule in all educational institutions to enter against each student on admission if he or she is milk shy—milk shy children being recognized as potential cases of tuberculosis. All children, and particularly the milk shy ones, are compelled to drink at lunch time a regulation ration of milk, and the subsequent improvement in the general health has been remarkable. To those adults who cannot drink milk, cheese or any solid preparation of milk like curds or chhana (as prepared in Bengal) make splendid substitutes, supplying all the food elements which go to make up the perfect food that milk really is.

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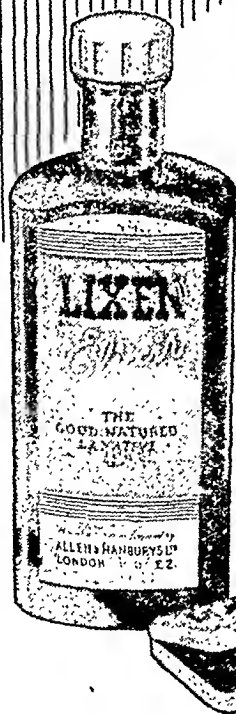
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The acidity of the human stomach is 0.2 per cent and not 0.4 to 0.6 (Colonel Cox's figure) though in excessive meat eaters it may be high; that of the cat is 0.35, of the dog 0.55, of the goat 0.044, of the horse 0.02, of the calf 0.15; in the monkey the figures are said to be similar to man's. Do not these figures suggest that man's diet should be more like that of the monkey than that of either cat or cattle? The monkey is not, *pace* Dr. Aykroyd's laboratory experiment, a meat eating animal. It lives wholly on fruits, nuts and vegetables although it may be insectivorous at times. Dr. Aykroyd's unfortunate *Macacus sinicus* who died of enteritis because he would not eat meat is by no means unique among monkeys in his antipathy to meat. Colonel Cox may have seen monkeys crushing birds with their hands before eating them and they may take kindly to meat in Dr. Aykroyd's laboratory, but in their natural habitat they seldom do and if only Colonel Cox could see them free in Northern India in and about towns or jungles he would certainly put the monkey among pre-eminently herbivorous animals and admit that they are none the worse for being herbivorous. It would be unfortunate if a scientist of Colonel Cox's standing should generalize from the disabilities of one unfortunate *Macacus sinicus* as he appears to have done from his sheep dog which immediately developed carbuncles on biscuits and rice.

Another argument of Colonel Cox's in favour of a carnivorous diet is its tradition as a protection against tuberculosis. Surely Colonel Cox is not unaware that if there is any traditional protector against tuberculosis in our dietary, it is the fat element and not protein. The pre-eminent position of cod-liver oil and butter has never been questioned in tuberculosis. If Knud Fabers' important work in Denmark on the Post-War (1914-18) incidence of tuberculosis in Denmark seems to support Colonel Cox, Hindhedi's equally authoritative work does not.

Indeed it is now (*British Medical Journal*, 8th May, 1943) the consensus of opinion that it is the energy value of a food that matters as protection against tuberculosis and that proteins are of no special help. The *British Medical Journal* goes on to point out that Dr. George Day's most recent work at the Mundesley Sanatorium assisted by the Medical Research Council goes even further and actually seems to suggest that the most valuable element may well be the despised carbohydrates.

Colonel Cox has decided in favour of a carnivorous diet for men on the close resemblance of the human gastro-intestinal tract to that of carnivora. The human stomach and cæcum are certainly unlike that of bovines, but is it so very unlike the equine stomach and cæcum? And are not the simian stomach and cæcum very close to the human organs, much closer than that of felines or canines?

Man has certainly travelled millions of years since he is said to have lived on the chase, though it is very doubtful if, except in a few degenerate races, man ever did live on the chase as pictured in European traditions of the cave man and not on fruits, nuts and vegetables as his collaterals still so largely do. Even if that idyll of Colonel Cox's ever was a reality, is it not the case that with the partial abandonment of carnivorous habits there has been a considerable improvement in physical efficiency since the time of the cave man? And are there not other things than mere physical efficiency which may have some value even to theorists of evolution? Three acres and a cow will keep a herbivorous family, but ten acres will not serve to maintain a carnivorous one. If a herbivorous family can be happy on three acres, a carnivorous one will not be happy even with ten. Does it not stand to reason that if every individual of a nation or race is carnivorous, the amount of lebensraum required will be multiplied at least three times, and would it not explain much of the aggressiveness and consequent devastating wars that have been a feature of humanity since the dawn of history? It is this instinct of self-preservation that has fostered those sectarian and religious prejudices advocating herbivorism that Colonel Cox deplures, and

their weakening has been coeval with a phenomenal increase of carnivorism with sadistic brutality as its most dominant feature—a reversal to virtual cannibalism.

The massacres and orgy of rape at Nanking, daily murders in cold blood of Poles and Czechs in their thousands, attempts at obliteration of Jewry in the whole of Eastern Europe, erasing of complete villages like Lidice, campaigns of mass sterilization of whole people—such foul deeds far surpass whatever might have been done by an Attila or Nadir Shah. Such events are not isolated from the general reversion to carnivorism and the making of physical efficiency as a fetish. Thus it has been estimated that the consumption of meat in America has gone up 400 per cent in the last 100 years. Attempts to demonstrate the uneconomical character of feeding corn to the cattle, and then eating them instead of eating the corn off the cob meet with little response.

The German Red Cross Society may say in its pamphlet—How to keep well—'meat though held in high favour is not an absolutely necessary article of diet' and again 'the best beverage is milk'. But these fall on deaf ears. In the late twenties the number of cattle slaughtered in Calcutta principally in one slaughter house (Tengra) used to be near about a lac (96,000) per year. It is now estimated to be not less than 800,000 per year and may even approximately reach the million figures at the present moment.

Carnivorism now stalks the world. Even the last citadel of vegetarianism, the Hindu in India, knowing full well how his diet has maintained him in moral and physical efficiency through ages when races who were his compeers have disappeared off the face of the earth, is learning to give up his vegetarianism.

Colonel Cox need not be despondent. *Homo sapiens* will justify his name and in his sapience will rather die in mutual slaughter than in extinction through natural evolutionary process.

NALINI RANJAN SEN GUPTA,

M.D., F.S.M.F.

91, CHOWRINGHEE,
CALCUTTA,
30th July, 1943.

HEMERALOPIA

SIR,—With reference to your editorial note on 'Hemeralopia' in the July 1943 number of the *Indian Medical Gazette*, I wish to draw your attention to 'Fuch's Diseases of the Eye—Brown—Tenth Edition', pages 412 to 415, wherein he recognizes Hemeralopia and Nyctalopia as different clinical entities. Under 'Hemeralopia' (night blindness) he says 'The patients state that they see normally well during the day but during the evening must be led along in less well illuminated streets, etc.'. Under 'Nyctalopia' he says 'The symptom opposed to that of hemeralopia is nyctalopia, i.e. that condition in which during the evening (in reduced illumination) one sees better than in bright daylight, etc.'.

The *British Encyclopædia of Medical Practice*, Vol. II, page 411, makes the point more clear. This says 'Nyctalopia—night vision—is a condition in which the sight is better at night or in semi-darkness than by daylight. Hemeralopia—day vision or night blindness. The sight is good by day or in a strong light, but fails at night'.

Through misuse in modern times these two words, 'Nyctalopia' and 'Hemeralopia', have come to mean the precise opposite of what their derivation from the Greek implies. The proper derivation of Nyctalopia is . . . meaning night blindness. Hemeralopia is derived from . . . meaning day blindness. Gould's *Medical Dictionary*, edited by Scott, second edition, 1928, says 'that an attempt to reinstate the ancient usage of these words can only result in confusion and they should therefore never be used'.

In view of the above, won't your proposal to use in your journal these words in the sense indicated by Stedman lead to some confusion in the medical, especially ophthalmic, world?

P. BALAKRISHNA MENON,

M.B., B.S., L.O.,
Eye Specialist.

CALICUT, MALABAR,
S. INDIA,

12th August, 1943.

[Note.—We thank our correspondent for this note. He and the authorities he quotes agree with our view that the word hemeralopia should mean 'day blindness' and not 'night blindness', and that the correct word is nyctalopia, which however is often used for day blindness. He apparently approves of Gould's suggestion that any attempt to correct the mistaken use of these words is now inadvisable. Perhaps it is, but this attempt is being made by various writers as well as ourselves.

Probably in the circumstances it would be best to avoid entirely the use of both words, and to use the English words 'day blindness' and 'night blindness'. These words are not scientifically accurate, for there is not a total loss of vision; but at any rate the words do not mean the exact reverse of what they should mean.—EDITOR, I. M. G.]

ANÆSTHESIA IN DISTRICT HOSPITALS

SIR,—The article by Lieut.-Colonel Cox in the August issue of the *Indian Medical Gazette* emphasizing the dangers of chloroform anæsthesia deserves wide publicity in this country where the subject of anæsthetics and their administration appears to be badly neglected in the medical curriculum. Unlike many other highly necessary reforms, improvement in this branch of medicine does not necessitate a large expenditure of public money.

Lieut.-Colonel Cox quite rightly condemns the almost universal use in this country of chloroform as a general anæsthetic agent. With this I am in complete agreement although I am sufficiently old fashioned not to advocate its complete abolition.

As a physician obliged—certainly not 'doomed'—to give anæsthetics, I have acquired a fair degree of familiarity with various kinds of anæsthetics (excluding those recently introduced) and methods of administration both in this country and in England. I have come to the conclusion that the simplest and safest anæsthetic for the ordinary doctor is open aether. I was extremely surprised to see that Lieut.-Colonel Cox apparently agrees with the generally held belief that

the use of aether as an anæsthetic in the tropics is impracticable, for he writes '... ether can scarcely be stocked, let alone used, on account of its volatility'. At the Kolar Gold Field Hospital about 250 major operations are performed every year, and for many years now the majority of these operations have been done under aether anæsthesia. Deaths on the table have been a great rarity, in spite of the fact that many patients were serious surgical risks. It is true that a little more aether is used than would be used for comparable cases in a non-tropical climate especially during the hot weather (D.B. temperature about 100°F.), but this does not interfere with efficient anæsthesia. There has certainly never been any difficulty in storing bottles of aether.

What is surely urgently needed here, is the training of medical men in the administration of simple and safe anæsthetics. Complicated machinery should be left to the expert. The anæsthetic of choice is obviously open aether, the materials required are simple and are easily transported, mask, lint or gauze (sufficient to make a thick pad), drop bottle and an airway—a gag and tongue forceps are useful in emergencies. The only disadvantage of aether is its unsuitability for induction. Every surgeon and anæsthetist appreciates the importance of a smooth induction in successful anæsthesia, and it is admitted that aether induction is laborious and unpleasant. A dilute chloroform-aether mixture is however tolerated very well. I use CHCl₃ 2 drachms to E. 2 oz., and when given slowly is extremely efficient and safe. It is fully realized that even small quantities of chloroform are dangerous, but when used carefully the risk is justified. I might add that from the point of view of the smoothness and rapidity of the induction I prefer the above mixture to either nitrous oxide or ethyl chloride.

I have referred to the necessity of an airway in the armamentarium of the giver of anæsthetics, it is surprising how rare an object it is in this country. The dictum 'keep the airway clear' should be posted in large letters in all operating theatres, and if open aether were generally adopted and an airway used in all cases, the surgeon could devote all his time to the operation and the framed orders of Hamilton Bailey on resuscitation of 'deaths on the table' could be relegated to an inconspicuous corner of the theatre.

It is time the aether bogey were laid. Aether can be used as an anæsthetic in almost any part of India most months of the year, and in South India (especially the Nilgiris) throughout the year.

A. CAPLAN, M.D., M.R.C.P.

THE KOLAR GOLD FIELD,
CHAMPION REEFS P. O.,

SOUTH INDIA,
29th August, 1943.

Service Notes

APPOINTMENTS AND TRANSFERS

COLONEL A. H. HARTY, C.I.E., returned from 4 months' leave and resumed charge of the office of the Inspector-General of Civil Hospitals, C. P. and Berar, on the afternoon of 4th August, 1943, from Lieutenant-Colonel N. S. Jatar, C.I.E., D.S.O., I.M.S. (Retd.).

Lieutenant-Colonel S. L. Bhatia, M.C., is appointed to officiate as Deputy Director-General, Indian Medical Service, with effect from the afternoon of the 31st July, 1943, vice Colonel J. B. Hance granted leave.

Lieutenant-Colonel G. Verghese, C.I.E., I.M.S. (Retd.), is appointed temporarily as Assistant Director-General, Indian Medical Service (Recruitment), with effect from the afternoon of the 10th August, 1943, until further orders.

Captain D. H. Harrison is appointed to officiate as Medical Officer for the Khorasan Agency and *ex-officio* Vice-Consul, Zahidan, with effect from the forenoon of the 17th July, 1943.

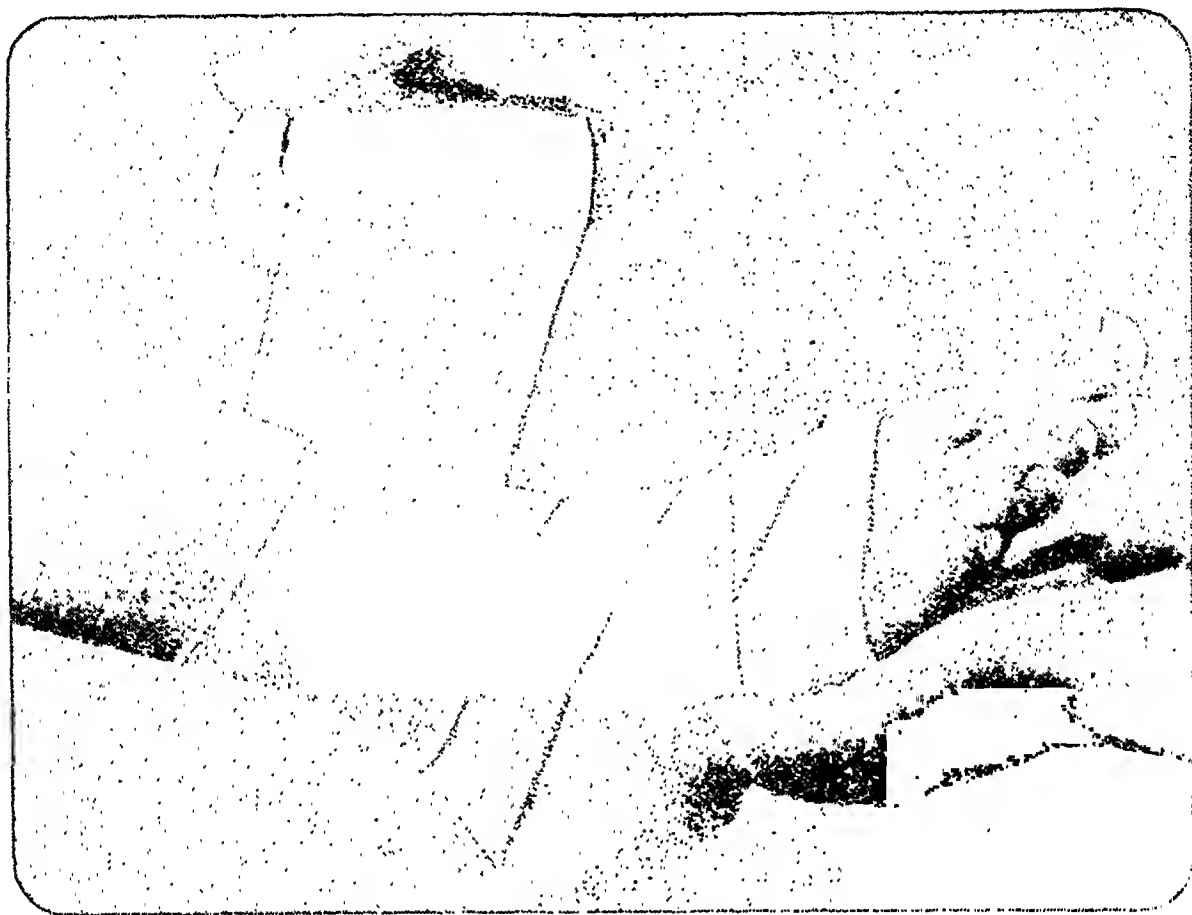
The undermentioned officers are transferred to the General Service cadre, with effect from the dates shown against each:—

INDIAN LAND FORCES

INDIAN MEDICAL SERVICE—SECONDED TO INDIAN ARMY
MEDICAL CORPS

(Emergency Commissions)

Captain P. S. Anantharaman. Dated 24th July, 1943.
Lieutenant John Francis Bonjour. Dated 8th June, 1943.



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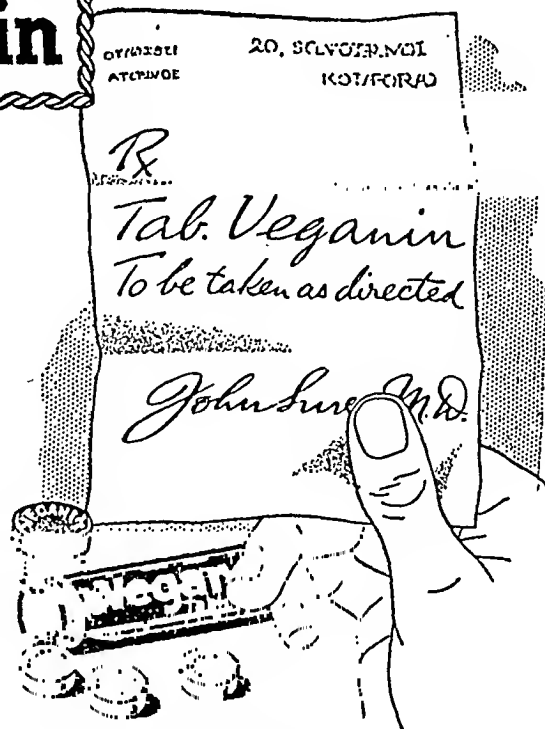
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Captain Jugraj Sanghavi. Dated 21st August, 1943.
 Captain M. A. Narayana Iyengar. Dated 8th July, 1943.

Lieutenant Ghanasyam Das. 28th July, 1943.

INDIAN LAND FORCES

INDIAN MEDICAL SERVICE—SECONDED TO INDIAN ARMY
 MEDICAL CORPS

(Emergency Commissions)

To be Captains

Nariman Shapurji Variava. Dated 25th June, 1943.

7th July, 1943

Eleyedath Kunhi Krishna Menon.
 Gummidipudi Chengalraya Sudarsanam Naidu.
 Puran Chand Khanna.
 Tevur Ramanatha Iyer Maniyan. Dated 19th July, 1943.

Surendra Kumar Dey. Dated 7th August, 1943.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE

(Emergency Commissions)

SECONDED FOR SERVICE WITH THE ROYAL INDIAN NAVY

To be Captains

Nasir Uddin Ahmad. Dated 19th February, 1943.
 Arcot Venugopal Madangopal. Dated 11th March, 1943.

21st July, 1943

Kawas Nowrosji Daria.
 Ramkrishna Shamrao Velaskar.

To be Lieutenant

Krishnarao Shantaram Dabholkar. Dated 19th February, 1943.

SECONDED TO INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

To be Captains

Hari Prakash Lal. Dated 3rd July, 1943.

7th August, 1943

S. K. Visveswar. Sadras Purushotham.
 Sadasiv Shankar Mhalas.

To be Lieutenants

7th July, 1943

Koka Dattatreya. Madan Gopal Anand.
 Varanasi Mohan Rao. Dated 7th August, 1943.
 Douglas Ashley Hugh Walton. Dated 18th August, 1943.

(WITHIN INDIAN LIMITS)

To be Captain

Goda Surya Narayana Murti. Dated 7th July, 1943.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE

(Emergency Commission)

To be Captain for Service with Royal Indian Navy
 Barjor Ardeshir Daruvala. Dated 26th July, 1943.

(WOMEN'S BRANCH)

To be Captain

(Miss) Harbans Kaur Grewal. Dated 3rd July, 1943.

To be Lieutenant

(Miss) Lila D. Karnick. Dated 19th July, 1943.

Lieutenant A. C. Sinclair is appointed to hold charge of the Medical Store Depot, Madras, with effect from the 6th September, 1943, vice Major W. T. Taylor granted leave.

The undermentioned officer reverts from the I.A.M.C. and is seconded for service in the Indian Air Force :—
 Lieutenant V. B. Tawadey. Dated 9th August, 1943.

To be Lieutenants

Meredith Carlyon Joseph Masters. Dated 3rd June, 1943.

Wilfred Ian White. Dated 1st July, 1943.

7th July, 1943

Byrappa Marisiddappa.	Syed Ziaul Hasan.
Sri Kishen Jetley.	Khurshid Ahmad Sheikh.
Uma Shankar Notyal.	Mian Abdul Aseem Aziz.
Ghulam Nabi Dar.	Shaikh Manzarud Din
Mohd. Sharif Ahmed.	Ahmad.
Ghulam Mohy-Ud-Din.	Mohammad Akram Alvi.
Dilbagh Rai Bhasin.	Narindar Singh Brara.
Krishan Lal Chopra.	Ghulam Akbar.
Som Parkash Kalsy.	Amrik Singh.
Mohammad Naqi.	Mohammad Aslam.
Sheikh Mohammad Salim.	Rafique Ahmad Khan.
Mangal Sain Malhotra.	Mohammad Ismail.
Mohd. Shafqat Ali Wasty.	

8th July, 1943

Jas Raj Kumar. Om Prakash Malhotra.
 Om Parkash Khanna. Faiz Ali Shah.
 Nawab Khan. Dated 14th July, 1943.
 Clifford Owen Bedell. Dated 20th July, 1943.
 Denzil Ian Gantzer. Dated 21st July, 1943.

7th August, 1943

Jai Krishna Jindal. Vidya Bhushan Kalra.
 Harnam Singh Seth.

PROMOTIONS

INDIAN MEDICAL SERVICE—SECONDED TO INDIAN ARMY
 MEDICAL CORPS

Lieutenant-Colonel to be Colonel

P. Savage. Dated 6th March, 1943.

LAND FORCES

INDIAN MEDICAL SERVICE—SECONDED TO INDIAN ARMY
 MEDICAL CORPS

(Emergency Commissions)

Lieutenants to be Captains

28th May, 1941

N. C. Chatterjee.	M. H. Alvi.
S. Pichumani.	P. B. Menon.
S. Rodrigues.	A. G. Menon.
K. L. Datta.	N. Sen Gupta.
L. S. Nathan.	A. L. Som.
A. Das.	A. S. Choudhuri.
S. G. Gnanaswaran.	R. B. Sule.
D. J. Shroff.	K. C. Dobhal.
S. L. Rikhye.	A. K. Sen Gupta.
V. P. Patel.	C. M. Desai.
J. R. Sen.	S. Banerjee.
P. G. Rau.	A. B. Roy.
M. K. K. Menon.	M. G. Hyder.
V. R. Kamath.	S. C. Bose.
T. K. Narayanan.	N. S. Gaitonde.
S. C. Ray.	R. Khan.
S. N. Chatterjee.	R. V. B. Tampi.
S. C. Roy.	H. C. Paul.
N. K. Roy.	A. H. Hamid.
R. M. Nadkarni.	A. I. Lakshminarayanan.
R. K. Satija.	V. R. M. Sadasivan.
B. N. Trilokekar.	S. D. N. Sinha.
N. A. Kuraishy.	S. C. Sarkhel.
J. Jacob.	S. K. Ghosh.
B. Mukerji.	M. M. Sharif.
K. S. Pillai.	N. A. A. Khan.
P. M. Bhandarkar.	D. R. Vaidya.
Y. K. C. Pandit.	T. D. Taravanar.
N. Dutt.	M. M. R. V. A. Nam-
S. V. Kail.	biyar.
S. R. Chowdhury.	T. V. R. Wariyar.
G. L. Dutt.	Y. S. Bawa.
M. N. Menon.	M. A. Paul.
P. C. Koshy.	C. C. Menon.
M. Aslam.	A. K. Dutt.

A. K. Mallik.	P. C. Nadungadi.
T. Titus.	S. A. Sheikh.
B. Ghosh.	K. G. Koshi.
H. L. Sah.	B. Singh.
S. K. Misra.	S. S. A. Khan.
G. Kumar.	R. D. Kamat.
R. S. Rao.	N. Rangavadivelu.
S. M. Q. Hoda.	E. R. Menon.
A. K. Bose.	K. S. Bhushanam.
J. J. Dharamraj.	K. R. R. Rao.
C. S. Krishna Murthi.	M. Imaduddin.
D. S. Shukla.	M. S. R. Roy.
B. M. Ambady.	N. K. Money.
G. V. Munje.	N. E. Sarangapany.
S. P. Mukherjee.	S. N. Mukerji.
U. P. Das Gupta.	R. A. Riyaz.
K. C. Dube.	M. K. Chaudhary.
Saligram Kaul.	H. Sen Gupta.
T. U. Poonen.	C. Bhadrachari.
S. P. Ramakrishnan.	A. K. Barat.
M. Abbas.	S. Parkash.
M. Said.	S. N. Sharma.
M. G. Pendharker.	I. G. Sastry.
R. R. Reddi.	S. G. Rajagopal.
S. K. Sen.	B. K. Bhadury.
A. P. Ray.	D. C. Roy.
S. C. P. Sinha.	M. Ramzan.
S. H. A. Gardezi.	T. K. Rithuparnan.
V. Rajagopalan.	G. S. R. Reddi.
O. Francis.	A. A. Khan.
H. A. S. Joseph.	M. Y. Qureshi.
P. K. Paul.	I. C. Misra.
R. Subramanian.	J. M. Sinha.
E. R. F. Rebello.	Nazir Ahmad.
S. Kesavulu.	G. Singh.
S. N. Narula.	B. P. Sinha.

N. F. Lilauwala. Dated 5th June, 1941.
B. K. Sheorey. Dated 23rd June, 1941.

2nd June, 1941

B. B. Chatterjee. G. B. Godbole.
S. V. Ghurye.

5th June, 1941

C. S. Venkatasubramaniam. M. C. Muniswamy.
maniam. M. C. Sheno. R. K. Chettur. Dated 6th June, 1941.
T. S. Row. Dated 2nd July, 1941.

5th July, 1941

V. K. Row. R. Krishnamurti.
J. K. Sarkar. B. A. Rao.
M. S. Mahadevan.

6th July, 1941

P. R. Dutt. C. F. Varied.
R. S. Hoon.

15th July, 1941

K. K. Bhatt. R. L. Pathak.
A. Hasan. R. S. Verma.

1st August, 1941

M. S. Kapur. M. P. Misra.

5th August, 1941

V. P. Rao. F. C. Mukherjee.
P. O. Ittooppunny.

G. S. Singh. Dated 6th August, 1941
P. P. Rit. Dated 15th August, 1941.
F. N. Shroff. Dated 1st September, 1941.
S. K. Puri. Dated 15th September, 1941.

5th October, 1941

A. G. David. R. M. Nair.
M. W. William. A. Krishnaswami.
V. P. S. Sarma. A. Ghaffar.
A. R. Subrahmanyam. M. C. Menon.

H. M. Rao. Dated 6th October, 1941.
T. M. B. Nedungadi. Dated 12th October, 1941.

5th November, 1941

V. S. Ramaswami. K. N. Ghose.
D. T. Gandhi. F. M. James.
V. Swaminathan. M. P. Verma.
G. Ahmed. M. I. Khwaja.

6th November, 1941

V. K. Vaidyer. V. S. S. Ramaswami.
C. M. Menon. M. Tajuddin.
J. G. Webb. Dated 3rd April, 1942.
J. D. C. Currie. Dated 6th April, 1943.
L. E. B. Gow. Dated 21st September, 1942.
K. Sukumaran. Dated 5th October, 1942.
B. Ghosh. Dated 16th December, 1942.

(WOMEN'S BRANCH)

Lieutenants to be Captains

(Miss) B. F. Thomas. Dated 17th October, 1942.
(Miss) L. James. Dated 27th April, 1943.

RETIREMENT

Colonel A. C. L. O'S. Bilderbeck. Dated 22nd August, 1943.

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The Editors of *The Indian Medical Gazette* cannot advise correspondents with regard to prescriptions, diagnosis, etc., nor can they recommend individual practitioners by name, as any such action would constitute a breach of professional etiquette.

Original Articles

'EOSINOPHIL LUNG'

By R. N. CHAUDHURI, M.B. (Cal.), M.R.C.P. (Edin.),
T.D.D. (Wales)

Assistant Professor of Tropical Medicine, School of
Tropical Medicine, Calcutta

THERE are several conditions which are known to cause an increase of eosinophil leucocytes above the normal, but in recent years a remarkable syndrome has been described, not so well known, which is characterized by massive eosinophilia with focal broncho-pneumonic infiltrations affecting both lungs and general symptoms such as fever and loss of weight. Without a blood examination the condition is apt to be missed and mistaken for tuberculosis of the lungs. The following case report may therefore be of interest:—

A Mohammedan male, aged 31 years, was admitted under the author into the Carmichael Hospital for Tropical Diseases on 22nd July, 1943, complaining of fever without remission for three days. He also had a troublesome cough.

History.—About eighteen days before admission, the patient had an attack of fever of a remittent type. After four or five days he developed a dry and irritant cough. The fever subsided on the tenth day, but the cough persisted, and he felt very weak. There was some loss of weight and he thought that he had an attack of influenza. After about a week he began to have fever again. It was on the third day of this fever that he was admitted into the hospital. His cough became worse and was troublesome at night, disturbing his sleep. At times it caused shortness of breath with inspiratory dyspnoea.

Personal history.—The patient was a clerk by occupation, living in Calcutta for the past fifteen years. There was no history of chest disease in the family. He was subject to frequent attacks of cold and cough especially during the rainy season since 1937, but as a rule kept good health during the winter months. Except malaria in 1929 he had no illness of importance in the past.

Examination

The patient was sparely built and weighed 88 pounds. The temperature on admission was 101°F., pulse rate 120 and respiration 28 per minute. He did not look very ill. He had a dry cough which was very irritant at times. The chest movements were symmetrical. Fremitus, resonance and breath sounds were normal. A few râles and ronchi were audible behind, especially at the right base. There was nothing of importance in the ear, nose and throat except that the right maxillary antrum appeared dull on trans-illumination (later it was explored but the result was negative). The heart was normal; blood pressure—systolic 115 and diastolic 80 mm. of Hg. The tongue was coated and moist. The appetite was poor, and bowels constipated. The spleen and liver were not palpable. There was no glandular enlargement. He had a certain amount of anxiety neurosis from fear of tuberculosis, and complained of sleepless nights apparently due to cough. The reflexes were normal.

Investigations

Blood.—Total white cell count—29,500 per c.mm.
Differential white cell count:—

	Per cent.	Per c.mm.
Neutrophils ..	16.5	4,867.5
Lymphocytes ..	6.5	1,917.5
Monocytes ..	1.5	442.5
Eosinophils ..	75.5	22,272.5

No immature cells were seen.

Hæmoglobin (Hellige)—13.8 grammes (100 per cent).

No parasites were found. The blood culture was sterile. The Wassermann reaction was negative. The erythrocyte sedimentation rate was 86 mm. in one hour (Westergren).

Sputum.—Three direct smears showed no acid-fast bacilli.

Stool and urine.—No abnormality.

The Mantoux test.—(0.1 c.cm. of old tuberculin, 1 in 1,000 dilution) was 'doubtful' positive.

X-ray of the chest.—'Diffuse mottling throughout both lungs suggestive of miliary tubercle' (figure 3, plate XXIX).

Diagnosis

The main clinical features of the case were fever, cough and loss of weight. The routine blood examination surprised us by the presence of massive eosinophilia. As there were lung symptoms, a radiogram of the chest was taken, and this gave rise to another surprise, as it was suggestive of miliary tuberculosis. The patient however was not ill enough for acute miliary tuberculosis. The possibility of chronic miliary tuberculosis was considered, but in this case we would expect some of the lesions at least to be calcified. Moreover, a high eosinophilia is not a feature of this condition. Naturally, bronchial asthma was considered to be another possible cause, but the clinical history, the absence of a typical attack and the radiological picture were really not suggestive of asthma. Helminth and syphilitic infections were easily ruled out. Pneumonoconiosis was another possibility, but it could be readily excluded as the patient had never been engaged in dusty occupations, and there was no sign of chronic fibrosis of the lungs. Pneumonoconiosis is not characterized by eosinophilia. There is also the Löffler's syndrome possibly caused by the migration of helminthic larvæ in the lung, but in this condition the infiltration in the lungs is transient and localized; it is usually discovered accidentally during mass radiography and is not associated with much general disturbance. The case under report showed no helminthic infection. Lastly, could it be eosinophilic leukæmia? This is an obscure and mysterious condition of which we have little or no experience. If it were true leukæmia we would however expect to find some immature cells, but none was found in this patient's blood on repeated examinations.

Thus it is obvious that in this patient we had to deal with a condition which could not be confidently classified under the usually recognized diseases. The signs and symptoms as observed in this patient however constitute a clinical syndrome of which a large number of cases have been encountered in this country, especially in South India, during the past three years. The condition has been variously termed, e.g. pseudo-tuberculosis of the lungs with eosinophilia, 'eosinophil lung', benign eosinophilic leukæmia or tropical eosinophilia,

Treatment

The patient was kept under observation for a week while various investigations were carried out. He had irregular fever during this period (*vide* figure 1). Next he was given a course of five

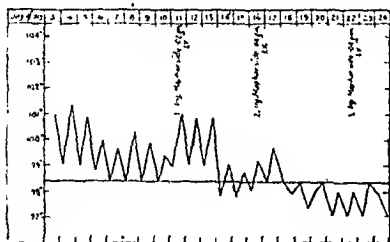


Fig. 1.

mapharside (Parke, Davis) injections intravenously. The first dose was 0.02 gm., and subsequently 0.04 gm. was given at intervals of about five days. He had nothing else but palliative treatment such as sedative linctus for cough and phenobarbitone for insomnia when required.

Progress

There was a feeling of well-being after the first injection, the temperature was normal soon after the second, and the cough which was very irritant subsided almost completely after the third injection. About the same time another skiagram was taken; it showed almost complete disappearance of mottling, but there were some hilar and peri-hilar markings with increased linear striations suggestive of chronic bronchitis. His general health improved and appetite returned. The leucocyte count was repeated every week with results as shown in the table below:—

TABLE

Date	3-8-43	10-8-43	16-8-43	25-8-43
Leucocytes:—				
Total count (per c.mm.) ..	14,000	13,500	10,600	6,200
Differential count:—	Per cent Per c.mm.	Per cent Per c.mm.	Per cent Per c.mm.	Per cent Per c.mm.
Neutrophils	15 2,100	29 3,915	55 5,830	50 3,100
Lymphocytes	14 1,960	12.5 1,687.5	14.5 1,537	26 1,612
Monocytes	1.5 200	2 270	3.5 371	8 496
Eosinophils	69.5 9,730	56.5 7,627.5	27 2,862	16 992
Sedimentation rate	16 mm.	10 mm.

The total white cell and eosinophil count and the erythrocyte sedimentation rate are represented graphically in figure 2.

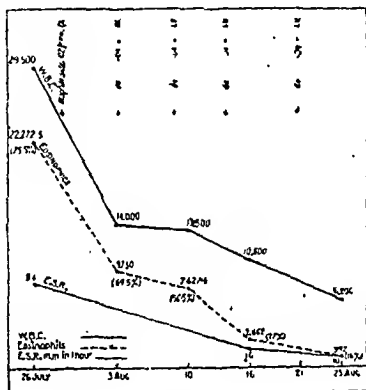


Fig. 2.

The patient was discharged apparently cured on 27th August with instructions to see us periodically. On

8th September, 1943, his total white cell count was about the same as on 25th August, and he had put on ten pounds in weight. Another radiogram of the chest was taken on 17th September: there was complete disappearance of mottling in the lung fields (*see* figure 4, plate XXIX).

Discussion

Frimodt-Møller and Barton (1940) described a 'pseudo-tuberculous' condition associated with eosinophilia. Their findings were based on an observation of a very large number of patients admitted into a sanatorium for suspected tuberculosis. They had fever, cough, loss of weight with high eosinophilia (the highest being 92 per cent), and diffuse mottling in the lung fields. The course was chronic and benign. The cases were carefully investigated, and they considered that the condition was possibly of allergic origin.

Weingarten (1943) described a similar condition which he called tropical eosinophilia, the symptoms being lassitude, fever and appreciable loss of weight within a short time followed by a dry irritant cough developing into typical bronchial asthma at times. The spleen was often enlarged. The most striking feature was, however, massive eosinophilia (in one case as much as 88 per cent), and this was responsible for considerable leucocytosis. The x-ray pictures showed disseminate mottling of both lungs.

Weingarten's observation was based on a study of a series of 81 cases affecting all races, age and sex. There was no evidence of familial, occupational or seasonal susceptibility. He was of the opinion that the condition was not an allergic state but put stress on the influence of environment as an aetiological factor.

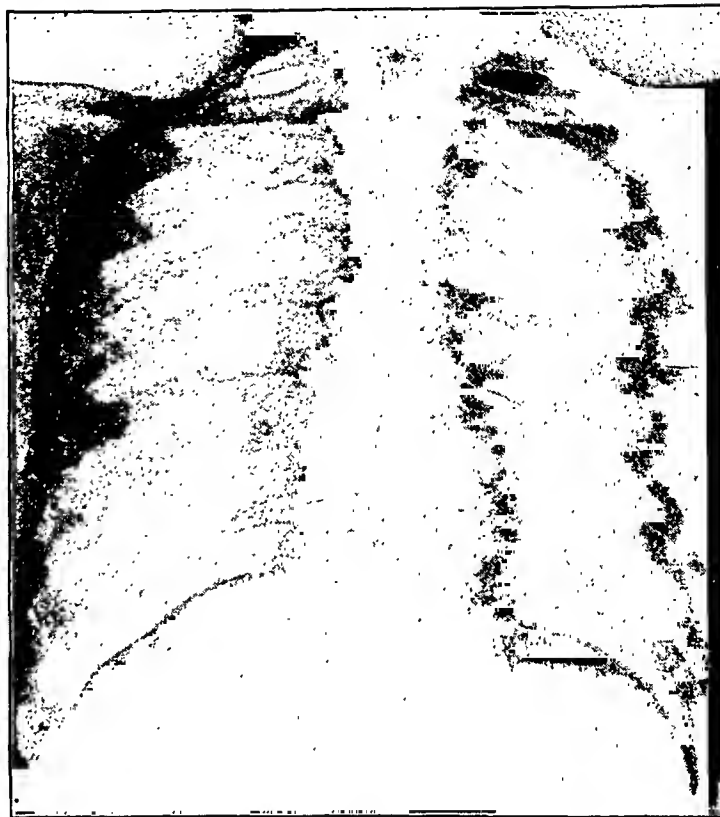
Simeons (1943) encountered 35 cases in nine years. The outstanding feature was febrile intermittent attacks of bronchitis often with symptoms of bronchial asthma. There was marked eosinophilic leucocytosis; many of the cells were highly lobed suggesting that these eosinophils reached a stage of development more advanced than that normally encountered. He considered this to be pathognomonic of this disease. Except in some cases the radiograms showed fine dissemination of nodular opacities evenly distributed over both lung fields. The spleen was distinctly enlarged in half of his cases.

Fig. 3.



Diffuse mottling in both lung fields.

Fig. 4.



Complete disappearance of mottling.

A SYMPTOMLESS CASE OF RENAL CALCULUS IN BOTH KIDNEYS : B. L. CHOPRA. PAGE 597.

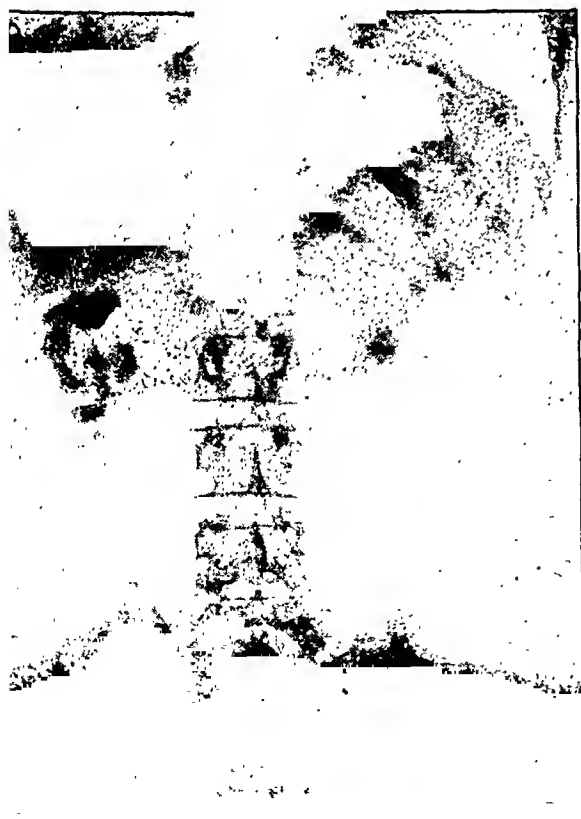
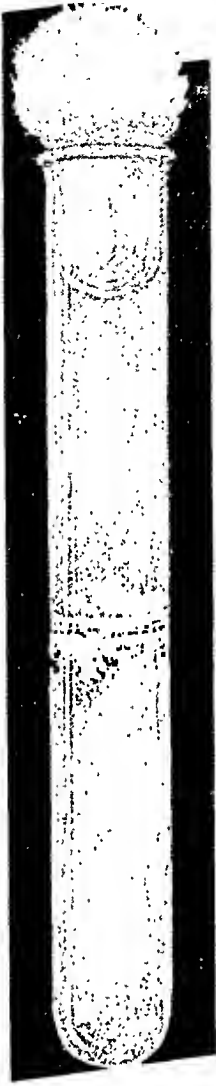


Fig. 1.



Fig. 2.

Fig. 1.



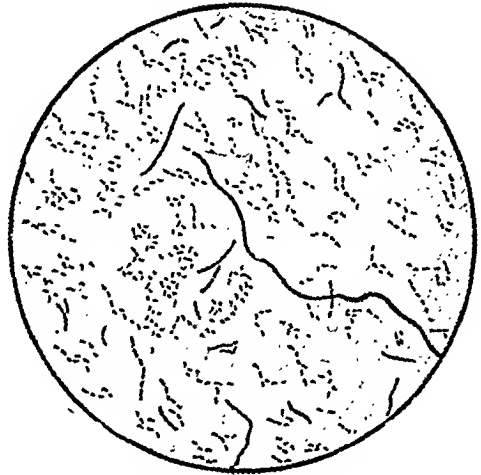
Glucose broth
12 days.

Fig. 4.



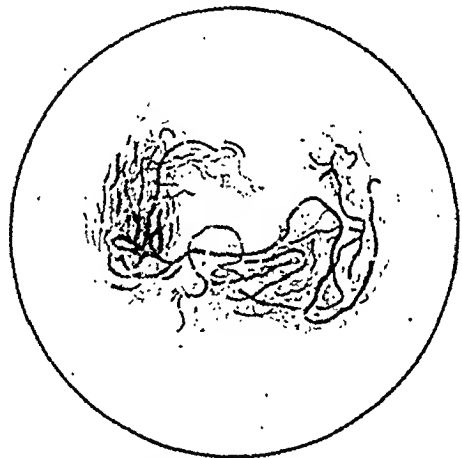
Natural size.

Fig. 2.



Potato media
4 days. $\times 450$.

Fig. 3.



Glucose broth
10 days. $\times 450$.

Fig. 5.



Section at the proximal end
of a piece of tissue coughed up.
 $\times 450$.

He used the term 'benign eosinophil leukæmia' for this condition.

As there has been no occasion for autopsy, the anatomical changes that give rise to the mottled appearance in the x-ray film are not definitely known. Perhaps there are two factors that take part in giving rise to this condition. The *primary factor* is the massive eosinophilia; this may be due to several causes. Some cases are probably examples of idiopathic eosinophilia; others are acquired on the basis of asthma, syphilis, blood diseases, trichiniasis, etc. Then there is a *precipitating factor* such as recurrent attacks of bronchitis. It is possible that widespread pulmonary infiltration of mature eosinophil cells with large granules is responsible for the radiological appearance in these cases. The presence of a large number of eosinophil cells in the sputum has been reported, but unfortunately in this case they were not especially looked for in the beginning, and, later, the patient had no sputum.

In treatment, organic arsenicals act as a specific. Weingarten at first tried various remedies for his cases but without a satisfactory result. One of them however contracted syphilis for which he gave nearsphenamine injections and was struck with their dramatic effect on the blood and x-ray picture. Subsequently he obtained uniformly good results with this form of treatment. Treu (1943) also reported two cases with similar results. Simeons treated his cases successfully with mapharside taken up in 10 per cent calcium gluconate solution; bi-weekly injections were given, four to six being usually required. He also observed that liver injections alleviated the clinical symptoms but the eosinophilia increased. A study of untreated cases showed that the condition gradually improved spontaneously, but the blood picture was never normal, and exacerbations occurred sometimes at very long intervals.

The present case had practically all the features of this syndrome. The eosinophilia was possibly idiopathic. The spleen was not palpably enlarged. The response to arsphenamine—clinical, hæmatological and radiological—was remarkable.

The condition is now well established as a clinical entity, and so far all the cases have been encountered in India only. In every case of chronic febrile cough for which no obvious cause is evident, it is worth considering the possibility of this condition.

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A NOTE ON A NEW STRAIN OF ACTINOMYCETES (*ACTINOMYCETES MUCOSUS* N. SP. BASU) OBTAINED BY BLOOD CULTURE FROM A CASE OF BRONCHIAL (?) ACTINOMYCOSIS WITH METASTASES

By CHARU CHANDRA BASU

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THE organism isolated appeared to involve primarily the bronchi with septicæmia and metastatic involvement of internal organs.

Clinical history.—The patient, a Bengali male, aged 45, used to get fits of cough about once a month, during which he coughed out soft whitish masses 1 to 2 inches long; this was followed by a slight amount of hæmoptysis. This went on for about a year. One day he had a sudden pain in the right kidney, followed by hæmaturia. At the same time he started running a temperature, and signs of bronchopneumonia were detected on physical examination of the chest. Two months later he had a recurrence of hæmaturia with pain in the left kidney. The fever continued; he developed peritonitis, and the case ended fatally 4 months after the first attack of hæmaturia.

Materials examined.—

- (1) Blood collected during the febrile period, following the first attack of hæmaturia.
- (2) Material coughed out.
- (3) Blood clots passed with the urine.

Blood culture.—The culture was done in glucose broth and, at the end of a week, a yellowish membranous growth was detected at the bottom. A small piece of this growth was washed in saline and was planted on agar and incubated for 4 days. Two types of colonies were seen. One was a yellowish slimy colony and the other an orange coloured colony. The slimy colonies consisted of Gram-negative bacillary organisms, which on further incubation showed filamentous forms, while the orange coloured colonies showed a Gram-positive diphtheroid organism which is still being studied. In the present article a brief description of the filamentous organism is given.

Cultural characters of the filamentous organism obtained from blood culture

The organism grew easily on all the usual laboratory media, under aerobic conditions at ordinary room temperature, though somewhat better at 37°C.

Culture on nutrient agar, blood agar, egg, potato and Sabouraud media.—Incubation showed fine punctiform colonies, lemon yellow in colour, in 24 hours. The colonies enlarged and became slimy in 4 days. Growths were not adherent to the media.

Synthetic agar and water agar.—Growths were scanty. *Deep glucose agar.*—Growth was practically confined to the surface.

Nutrient broth.—At first a turbidity appeared but gradually the broth cleared and a yellowish stringy deposit formed at the bottom.

Glucose broth.—Showed membrane formation at the surface (figure 1. plate XXX); these gradually sank to the bottom.

Litmus milk.—No clotting or acid formation. Yellow deposit at the bottom and yellow ring at the surface.

Sugar reactions.—No acid formation in arabinose, glucose, mannose, sucrose, xylose, lactose, maltose, inulin, raffinose, mannite and dulcitol in 3 weeks.

Peptone water.—Indol formation marked in 6 days.

Starch agar.—No hydrolysis.

Gelatine stab.—No liquefaction.

Tellurite medium.—Slight reduction.

Animal inoculation.—Subcutaneous and intraperitoneal inoculations into guinea-pigs were found to be non-pathogenic.

Micromorphology.—Smears from agar and blood agar culture at first showed Gram-negative bacilli (1.5μ to $2.5\mu \times 0.5\mu$), later on Gram-positive bacilli were also seen at first massed together. On further incubation these could be seen scattered among the Gram-negative bacilli, which, however, remained predominant. Gradually many of these on incubation showed filamentous forms, usually from 4μ to $5\mu \times 0.5\mu$, later on some very long forms up to 20μ were seen. Cultures on potato media showed long filamentous forms (figure 2, plate XXX). In egg media, old cultures showed Gram-negative coco-bacillary forms in predominance, though some bacillary and filamentous forms were also seen. Stained preparations from the surface growths in glucose broth showed only Gram-positive and Gram-negative filaments (figure 3, plate XXX).

The masses coughed out were about 1 to 2 inches long, pinkish in colour (figure 4, plate XXX). They had a loose texture at the distal end and were firmer at the proximal end. Sections at the proximal end showed loose granulation tissue, containing polynuclear cells, plasma cells and some vessels. Fine mycelial filaments were seen running in all directions (figure 5, plate XXX). Sections higher up showed a predominance of hyphal elements with a few leucocytes entangled in its meshes. Cultures from pieces showed various types of organisms, among which a filamentous organism similar to that obtained by blood culture was seen.

Sections of blood clots passed with the urine showed mycelial filaments running throughout the clot.

Summary of the bacteriological findings

The organism is difficult to classify and appears to belong to a new species. The particular features presented by the organism are the following:—

(1) Sections of the tissue coughed up showed fine mycelia.

(2) Cultures did not show substratum mycelia. No aerial mycelia formation was seen at any stage (during continuous observations for 4 years).

(3) Smears from 24 hours' culture showed Gram-negative bacillary forms. On further incubation, Gram-positive masses consisting of short Gram-positive bacilli appeared along with the Gram-negative forms. Subsequently these Gram-positive bacilli became longer in size and were found scattered among Gram-negative bacilli of various lengths.

(4) Gram-positive and Gram-negative filaments were seen in older cultures and in the surface growths of glucose broth cultures.

(Concluded at foot of next column)

DOES A HOOKWORM TOXIN EXIST?

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and

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MANY investigations have been devoted to the solution of the problem of the mechanism by which the hookworm exerts its deleterious effects. There is no doubt that the answer to the question is as complex as the syndrome produced by the hookworm. Loss of blood due to the sucking worm, increased by the prolonged oozing from the abandoned bites in jejunum and duodenum, is certainly one factor concerned in causing anæmia; this anæmia is responsible, due to the anoxæmia accompanying it, for the myocardial damage in the majority of cases. Many authors think that the amount of blood lost in this way is not sufficient to explain the extreme degree of anæmia which so frequently is encountered in ancylostomiasis, though the quantity of blood drawn by one worm daily is estimated as being between 0.38 and 0.84 c.cm. (cf. Strong, 1942). Since most of our hookworm patients suffer from malaria and from intestinal infections, and since many of them, especially women, are infected with *Escherichia coli*, the amount of blood lost as such is not the only factor influencing the anæmia and especially the capacity for blood regeneration. Malnutrition (Manson-Bahr, 1940), wrong food habits (Heilig, 1942) and multiple infection might depress the hæmopoietic capacity to such an extent that even a smaller amount of blood could not be replaced,

(Continued from previous column)

(5) Growths on solid media were soft and slimy and did not adhere to the medium.

(6) Gelatine was not liquified.

In a previous communication (Basu, 1937) a new species of actinomyces obtained by blood culture was reported by me, and this organism was named *Actinomyces sanguinis* N. Sp. Basu. At that time culture was sent to Miss D. Erikson who made a special study of the pathogenic organisms of the Actinomyces groups in the national collection of type cultures and published her observations in a special report (Erikson, 1935). She made a careful study of the specimen and placed it under Group I Orskov.

The present species appears to fall under Group II Orskov, and is provisionally named *Actinomyces mucosus* N. Sp. Basu.

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especially when the materials of hæmoglobin synthesis, iron and protein, are not sufficiently supplied and/or not properly utilized to make good the continuous drain extending over a long period.

Nevertheless, various theories have been advanced to meet the difficulty of explaining quantitatively the development of the severest degrees of hypochromic anæmia in cases in which, apparently, only minute losses of blood occurred.

Most of these theories have been based on the assumption that the hookworm produces one or more toxins, causing hæmolytic, paralysing the bone marrow, or exerting both these effects, so that a weakened hæmopoietic system would have to cope with an increased need for blood production; such a discrepancy between requirement and production capacity would easily explain the final negative balance. However, the existence of one of the two supposed factors, *viz.* increased blood destruction, was definitely disproved. Neither the motions nor the urine of uncomplicated hookworm anæmias contain an increased amount of urobilin, and the bilirubin content of the blood is low, facts which exclude any pathological degrees of hæmolytic (cf. Chandler, 1929; Djamil, 1924). Thus, if a toxic hookworm effect is at work at all, it necessarily acts by interfering with the normal function of the bone marrow; this eventually was investigated by De Langen (1924) who found that, in hookworm anæmia, the primary resistance of erythrocytes is equal to the secondary resistance in the fragility test which is due to the absence of young red blood cells; he concluded from this result that hookworm infection causes an aplastic anæmia by a toxic action on the bone marrow. De Langen (*loc. cit.*) himself provided a powerful argument against his conclusion by quoting Whipple, Hooper *et al.*, who stated that iron, arsenic, etc., were 'not able to establish the slightest effect' in aplastic anæmia. If this holds good for every kind of aplastic anæmia, hookworm anæmia certainly is not an aplastic one, no other anæmia responding so promptly to iron as does that of ancylostomiasis. Still less successful in proving the existence of a hookworm toxin were the attempts of De Langen's collaborators. Djamil (*loc. cit.*) estimated the renal function in ancylostomiasis and found a high value for Ambard's constant in eleven out of seventeen cases, independent of and not parallel with the degree of anæmia; some of his urea values are so improbable, and the experience is so general, that the kidney function is not impaired in plain hookworm infections, that his results are not convincing. Oudendal (1924) performed histological examinations of the intestinal wall in cases of ancylostomiasis, arguing that his findings were in favour of a toxic action. But the facts reported by him do not support such a conclusion. The lesions described and illustrated in his paper are not diffuse, as is expected when a diffusible toxin spreads through the tissues; they are almost confined to the site of the worm bite. De Langen (*loc. cit.*), however, was one of the first to recognize the importance of the dietary factor in anæmia prevention, and later (De Langen and Lichtenstein, 1936) he emphasized this point still more.

Thus, from all the supposed toxic activities of the adult hookworm, only one seemed to be established; extracts from the buccal end of the worms contain an anti-coagulant substance (Leob and Smith, 1940) which, probably, is responsible for the prolonged oozing of blood from the bites in the intestinal wall. The only other known, though not generally recognized, toxin is that by which the ancylostome larvæ produce the 'ground-itch' (Smith, 1906).

The toxin theory became so improbable that Scott (1938) pointed out that not the number of hookworms but the iron reserve of the host determines whether and to what a degree anæmia develops. In full accord with this opinion is the statement of Napier *et al.* (1941) that the main manifestation of hookworm disease, the anæmia, was merely due to iron deficiency, as proved by the amazing effect of iron medication on the blood picture prior to deworming in spite of undiminished worm infestation, and that the existence of a hookworm toxin is entirely hypothetical.

A revision of this position seemed required in the light of a new observation. Heilig (*loc. cit.*) found that out of 65 cases of severe hookworm anæmia and heart-muscle damage, six showed no improvement of the heart condition, clinically, radiologically and on electrocardiographic examination, in spite of a considerable increase of hæmoglobin and erythrocyte count, unless complete deworming was achieved; after expulsion of the worms, the heart condition improved rapidly, even when the hæmoglobin- and blood-figures remained constant. In the other 90 per cent of this series, the myocardial condition improved simultaneously with the blood status. The obvious conclusion seemed to be (1) that anæmia and the heart-muscle lesion are not caused by the same factor, (2) that anæmia is not necessarily the cause of the pathological heart condition, and (3) that something directly connected with the presence of the hookworm in some cases prevents the heart improvement, although an abundant supply of iron overcomes the deleterious effect of the parasite on the blood condition. It seemed desirable to find out whether the existence of such a myocardiotropic factor could be established by some direct proofs, based on a registrable effect. To this end the following investigations have been performed.

Methods of investigation

Twenty-six patients suffering from a severe hookworm anæmia but free from any other active disease have been selected and treated with massive doses of iron (Blaud's pills, 90 grains per day). At a hæmoglobin level of 35 to 40 per cent (Sahli) deworming was performed with carbon-tetrachloride and oil of chenopodium, and iron medication was stopped from one day prior to deworming up to the end of the investigation; thus, such changes as developed after deworming were not caused by any medication.

From the date of admission up to one week after deworming, hæmoglobin and red blood cells were estimated at weekly intervals. Electrocardiograms have been traced three times before starting treatment, one day before deworming, and again about one week after deworming. At the same three stages, blood serum was used for perfusing isolated frog hearts; at our request, the perfusion experiments

have been performed by Dr. G. S. Raghunatha Rao^{*}, assisted by Dr. N. Anandalwar[†], who are publishing their findings elsewhere in detail. Using Gunn's modification of Trendelenburg's method, the action of the frog heart, perfused with frog-Ringer-solution, was registered in the usual way. Only when a perfectly regular, normal action was established, the serum of our patients in various dilutions was substituted for the Ringer-solution. A serum concentration of one to one million was found most suitable to attain constant results and to exclude an unspecific 'serum effect'. As soon as a definite reduction of the heart amplitude was established on the graph, the frog heart was washed out with the physiological solution. To exclude fallacies due to spontaneous changes of the heart reactivity, only those experiments have been utilized in which complete recovery of the amplitude took place after renewed Ringer-perfusion; otherwise, the heart was discarded, and the same procedure was repeated with another one. Due to various circumstances, such as the impossibility of keeping the patients long enough after deworming, the lack of frogs at the required time, etc., all these investigations could be completed in only fourteen cases, all of the Hindu ryots (12 men and 2 women). The results are tabulated below.

Results.—On admission, the hæmoglobin content varied between 10 and 18 per cent (Sahli), the average being 13 per cent (Sahli). It took about three to four weeks of iron medication to increase this figure to such an extent (35 to 40 per cent) that deworming with carbon-tetrachloride could be performed without any risk. All the electrocardiograms taken before anti-anæmic treatment showed some damage of the myocardium. In two cases the lesion was slight (\pm), in seven (2 women) definite (+) and in five considerable (++). In five cases a definite (>), in six (2 women) a considerable (\rightarrow), improvement was noticed before deworming. In two of the first five, a further improvement took place after deworming. No improvement before deworming was found in three cases; one of them improved after deworming, two remained unaltered, but none of them showed a considerable cardiac lesion on admission. In all these cases the blood condition improved considerably before the elimination of the hookworms.

The serum toxicity was manifested by a well-marked reduction of the amplitude of the frog heart beat. In cases tabulated as ++ or +++, this diminishing of the amplitude was visible on direct observation of the heart; in those marked +, only the graph demonstrated it. The table shows that the depressant action of the sera on admission is not strictly proportionate to the extent of pathologic signs in the cardiogram. Of the two cases showing

cardiographically only slight damage, one gave a slight, the other a distinct (++) serum reaction. Of the seven definite (+) cardiographic lesions, four corresponded to the degree of serum toxicity, whereas three showed a higher degree (++) of depressant effect on the frog heart. Of the five cases with considerably damaged hearts, two showed serum of distinct (++) or considerable (+++) toxicity, whereas three belonged to the group of slight toxic sera.

The depressant effect of serum upon the frog heart disappeared before deworming, corresponding to the improved blood status in seven (2 women) and was diminished in another three patients; it remained constant in three cases. After deworming it disappeared completely in three cases, out of which two showed no change before. Only three sera retained some toxic effect even after deworming.

Discussion

Comparing the results tabulated here, with those of our previous report (Heilig, *loc. cit.*), we see that in eleven out of fourteen cases the heart condition, according to the electrocardiogram, improved simultaneously with the blood status in spite of the persistent worm infection. In addition, the perfusion experiments show that in eleven cases the serum toxicity disappeared or was substantially diminished when the blood condition improved before deworming. But here again a minority group remains, consisting of three cases (nos. 9, 12 and 14) in which the cardiogram was definitely improved, and of four cases (nos. 5, 9, 11 and 14) in which the serum toxicity was considerably diminished after deworming. One of the cases (no. 9) showed no cardiographic improvement one day after deworming, but a definite amelioration seven days later; two cases (nos. 12 and 14) a moderate cardiographic improvement before, a considerable one afterwards. In cases nos. 5 and 11, the serum toxicity was not influenced by the improvement of the blood condition but was abolished some days after deworming; in nos. 9 and 14 it was reduced before, but it disappeared one week after, anthelmintic treatment. The fact that in ten cases the development of the changes of electrocardiogram and of the heart depressant effect of serum correspond with each other, revealing a striking parallelism, favours the assumption that the factors responsible for them might have something in common. However, there are two cases (nos. 5 and 11) in which the cardiogram improved already before deworming, while the toxicity disappeared only afterwards; one case (no. 10) in which a slight toxicity (+) vanished when no changes were visible in the cardiogram; and, finally, one case (no. 12) showing a considerable cardiac regeneration, whereas the serum effect was only slightly reduced. It is not surprising that methods so different as electrocardiography and studies of effect of serum on the beat of the frog heart yield analogous results in not more than

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TABLE (for key see text)

Name, sex, investigation no.	Date	Hb% (Sahli)	R.B.C. (millions)	Cardiogram	Serum toxicity
K. G., ♂, 2738, no. 1.	1-6-42	13	1.01	damage ±	+
	29-6-42	45	3.15	impr. nil	+
	3-7-42	Deworming; worms	52		
	9-7-42	45	3.01	impr. nil	+
M., ♀, 4099, no. 2.	30-7-42	13	1.10	damage +	+
	8-9-42	35	2.61	impr. -	nil
	10-9-42	Deworming; worms	20		
	17-9-42	38	3.12	impr. →	nil
M. G., ♂, 4495, no. 3.	19-8-42	18	1.52	damage ++	+
	21-9-42	35	2.7	impr. →	nil
	26-9-42	Deworming; worms	++		
	3-10-42	40	3.2	impr. →	nil
R., ♂, 4615, no. 4.	26-8-42	15	1.31	damage ++	++
	21-9-42	40	3.2	impr. >	+
	24-9-42	Deworming; worms	++		
	1-10-42	50	3.7	impr. >	+
H. G., ♂, 4720, no. 5.	31-8-42	10	1.2	damage +	++
	28-9-42	40	3.4	impr. →	++
	1-10-42	Deworming; worms	+		
	5-10-42	40	3.3	impr. →	nil
Ke. G., 4930, ♂, no. 6.	14-9-42	12	1.02	damage ++	+
	31-10-42	37	3.01	impr. →	nil
	4-11-42	Deworming; worms	+++		
	14-11-42	40	3.2	impr. →	nil
V., ♂, 5042, no. 7.	21-9-42	16	1.05	damage +	++
	12-10-42	38	2.8	impr. >	nil
	13-10-42	Deworming; worms	++		
	15-11-42	43	3.2	impr. >	nil
A., ♂, 5754, no. 8.	22-10-42	13	1.05	damage ++	+
	9-11-42	38	2.6	impr. →	nil
	13-11-42	Deworming; worms	+		
	21-11-42	48	3.6	impr. →	nil
K., ♂, 5938, no. 9.	7-11-42	10	0.95	damage +	++
	30-11-42	35	2.44		+
	4-12-42	Deworming; worms	+		
	5-12-42	35	2.6	impr. nil	
	12-12-42	35	2.56	impr. >	nil
J., ♂, 6114, no. 10.	5-11-42	15	1.12	damage +	+
	1-12-42	43	3.26	impr. nil	nil
	2-12-42	Deworming; worms	+++		
	5-12-42	50	3.82	impr. nil	nil
Ch., ♂, 6381, no. 11.	17-11-42	11	1.02	damage +	+
	17-12-42	35	2.54	impr. >	+
	17-12-42	Deworming; worms	++++		
	24-12-42	42	2.98	impr. >	nil
Hy. G., ♂, 6509, no. 12.	22-11-42	15	1.12	damage ++	+++
	17-12-42	42	3.22	impr. >	++
	17-12-42	Deworming; worms	++++		
	24-12-42	60	..	impr. →	++
P., ♀, 6971, no. 13.	17-12-42	10	1.01	damage +	+
	7-1-43	40	3.23	impr. →	nil
	10-1-43	Deworming; worms	+++		
	16-1-43	48	..	impr. →	nil
Ka., ♂, 550, no. 14.	29-1-43	15	1.25	damage ±	++
	15-2-43	40	3.18	impr. >	+
	19-2-43	Deworming; worms	+++		
	26-2-43	50	3.72	impr. →	nil

71 per cent of cases, if it is permitted to express our small figures in percentage.

Returning to the question whether it is possible to distinguish between the effect of hookworm anaemia and that of another (toxic) factor upon the heart muscle, it seems that the present findings support such a differentiation. In cases nos. 9 and 14, the blood status did not improve, or only improved within the period during which the cardiogram became normal; however, as far as cardiographic changes are concerned, much more convincing cases have been reported previously (Heilig, *loc. cit.*). In cases nos. 5 and 9, the blood status remained constant, while the serum toxicity disappeared; in cases nos. 11 and 14 deworming improved the blood picture only to a moderate extent, whereas the serum effect was abolished.

These observations are difficult to explain if one assumes that the anaemia, with its consequences of anoxaemia, etc., alone is responsible for heart damage and toxic serum effect. There is no doubt that iron medication and blood regeneration cause a very considerable improvement of the myocardium and reduce or abolish the depressant effect upon the frog heart in a high percentage of cases. But the findings in the minority group, in which improvement is found on deworming and not on anti-anaemic treatment, make it probable that, apart from the anaemia, a myocardiotropic factor is present in the circulation, connected with the presence of the hookworm. In those cases in which improvement is achieved in spite of it, its effect is overcompensated for by blood regeneration.

The least probable interpretation of this agent is to call it a chemical toxin produced by the hookworms, all the previous investigations having failed to establish one, apart from an anti-coagulin. One could hardly think of such a compound not being an antigen, as few chemical toxins are, and yet being detoxified in most of the cases by iron or the improved blood condition. Another possibility is the lack of some factor less essential for blood than for heart-recovery; in this case, only those who are very sensitive to this deficiency or depleted of any reserves of this substance could not repair the heart lesion and not regain the serum balance unless the hookworms responsible for this condition are eliminated. McKenzie (1939) and Hoff and Shaby (1939) found that vitamin-B₁₂ deficiency is responsible for some manifestations of ancylostomiasis; these authors think that this lack might be caused or aggravated by the activity of the hookworms. One could imagine that such a disturbance in the co-enzyme system could influence the heart metabolism more than the bone marrow, and, due to dietary differences, affect one group of individuals more than another. The most probable explanation seems to be that the factor which damages the human heart muscle as well as depresses the beat of the frog heart is a toxin in the serological sense, serum anti-bodies having definitely

been established in dogs which were actively immunized with living ancylostome larvae (McCoy, 1931; Foster, 1935; Otto and Kerr, 1939; Otto, 1940). If such were the case, iron therapy or increased haemopoiesis would stimulate the anti-toxin production of the majority group to such an extent that all the free toxin was neutralized; in the minority group, due, perhaps, to a weakness of the reticulo-endothelial system, a surplus of circulating toxin would prevent recovery of the myocardium, and maintain the depressant serum effect, without being able to suppress blood improvement against the powerful stimulus of iron therapy; this effect could last as long as the toxin producer, the hookworm, is at work.

Concluding, we wish to point out that a fairly satisfactory solution of the hookworm toxin problem could be found by considering separately the aetiology of hookworm anaemia and the heart lesion. As far as the anaemia is concerned, the loss of blood which causes a continuous drain on iron and protein reserves explains its development. The insufficient iron and vitamin intake, a quantitatively and qualitatively unsatisfactory protein content of the foodstuffs consumed in those parts of the country where hookworm disease is most widely prevalent, make a repair of these losses impossible, unless proper treatment is applied. Malaria and infections of the urinary and intestinal tracts contribute to increasing the anaemic condition to extreme degrees. It is not necessary to add to these factors an anti-haemopoietic hookworm toxin, the existence of which is neither proved nor even probable. On the other hand, the fact that in certain cases myocardial damage and a heart depressing effect of serum persist in spite of a considerable improvement of the blood status, and that these pathological manifestations disappear within a short time after complete deworming, could easily be explained by some toxic activity of the hookworm. At present, a definite statement as to the nature of such a toxin is not possible. In our opinion, it is likely to be of antigenic character.

Summary

Fourteen cases of uncomplicated hookworm anaemia have been investigated before iron medication, at the end of the course of iron treatment before deworming, and one week after deworming.

Haemoglobin estimations and red blood cell counts have been performed at regular intervals, also cardiographic examinations and frog-heart perfusions with patient's serum before iron treatment, before deworming and one week after deworming.

The results were analysed and discussed.

The existence of a toxic influence of the hookworm upon the human heart muscle and the isolated frog heart seems to be probable.

(Concluded on opposite page)

CONCERNING THE WASSERMANN REACTION

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THE intention is to draw attention to (i) certain features of the technique, (ii) the false reactions, (iii) the Wassermann positive rate for Indians, and (iv) a new name for the Wassermann reaction, namely, Leeithin Complement Fixation (LCF).

I. Certain features of the technique

1. *The titrated controls.*—The usual positive control put up from a 1 in 5 dilution of a positive serum left over from the last test, or even intentionally collected and kept for some time, is a very poor control. Some positive sera give a complete fixation of the usual one or more MHD of the complement in a 1 in 200 dilution; others can do so in 1 in 5 dilution only. The margin of variation allowed for in this control, 5 to 200, is too wide to be useful in indicating whether the antigen-antibody systems involved in the reaction of complement fixation are

(Continued from previous page)

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working with the usual sensitiveness and specificity on a particular day.

The writer pools and preserves sera fixing 4 MHD of complement with an uncholesterinized antigen (Grevall, Das and Sen Gupta, 1938; Grevall, Chandra and Das, 1940). A 1 in 50 dilution of the pooled sera gives a complete fixation and a 1 in 100 dilution an incomplete fixation with the usual cholesterinized antigen and the smaller dose of the complement. Sometimes the potency of the serum is greater. The potency is determined by titration. It keeps unchanged until the serum is exhausted and yields repeatable reactions, day after day, for months.

It is pointed out that without the employment of titrated positive controls, the Wassermann reaction of borderline cases of syphilis is not repeatable and therefore not reliable.

The writer is aware of the reported seasonal variability of the Wassermann reaction (Hoverson *et al.*, 1935). He has, however, personal experience of the seasonal variability of the fixability of the complement. The latter variability must be excluded by the titration controls; otherwise an increase or decrease in the reaction of a serum may result from this cause alone; in fact the writer believes that more often than not it does so result.

2. *The complement.*—This reagent has six attributes which affect the reaction of fixation significantly. It may be (i) of high titre, (ii) of low titre, (iii) of optimal titre, (iv) cholesterol shy, (v) cholesterol fast, and (vi) of optimal reaction with cholesterol.

The optimal titre is given by 1 in 40, 50 and 60 according to the scheme of the British Method No. 4 (Medical Research Committee, now Council, 1918). Titres below 40 are low, and above 60 high. Other things being equal, low titre complements are fixed less and high titre complement more than the optimal titre complement.

The optimal reaction with the cholesterol is the one which makes the tubes in the two rows of the titration (with and without antigen) correspond, *i.e.* which ensures that neither more nor less than 1 MHD of the complement will be rendered inert by the cholesterol contained in the antigen. When more than 1 MHD is rendered inert, the complement is cholesterol shy; and when less than 1 MHD is rendered inert, it is cholesterol fast. Other things being equal, the shy complements are fixed more than the fast complements.

The complements displaying the four non-optimal attributes need special adjustments: the number of MHD used is increased or decreased and the cholesterol content of the antigen is raised or lowered. Very briefly, more is used of a high titre and less of a low titre complement than the dose indicated by the titration; less cholesterol is used than in the standard antigen with a shy complement; and either the number of MHD is decreased, or else phenol is added

to the antigen in the case of the fast complement (Greval, Chandra and Das, *loc. cit.*). With these adjustments, the titrated controls give the same reaction as they do with a complement of optimal titre and reaction. Even when the reaction of the controls falls short of the one expected, a measurement of the departure from the standard reaction is available.

3. *The antigen.*—In the writer's experience, it is not so much the type of the antigen as the quality which makes a significant difference in the fixation of complement. He uses three antigens routinely and four occasionally. They are: (i) plain alcoholic heart-extract antigen, (ii) McIntosh and Fildes' antigen, (iii) Bordet's antigen, and (iv) McIntosh and Fildes' antigen phenolized. The first three are used as routine, and the fourth occasionally, for clinically known cases only. The first, second and fourth antigens are made from the same source and third from a standard source.

The plain alcoholic heart extracts vary in their potency in reacting with the kind of serum which provides the titrated controls. In preparing the standard antigen, the extracts must be selected or corrected by concentration, pooled and tested. A reasonably high potency is aimed at and obtained (with a complement of optimal titre and reaction). A good extract fixes 4 MHD of complement with a 1 in 10 dilution of the serum.

McIntosh and Fildes' antigen is made from the plain alcoholic heart extract conforming to the standard. The phenolized antigen is made from the former.

Bordet's antigen is made from pieces of hearts (laid aside for the purpose) which have yielded the standard plain alcoholic extract without concentration. The quantity of this antigen required for the routine test is smaller than that of the others.

specific and differentiates less between new, old, treated and untreated cases; and (iv) the cholesterinized-alcoholic heart extract phenolized is almost as sensitive yet specific and differentiating.

4. *The rbc suspension.*—Other things being equal, the greater the density of the suspension, the bigger will be the quantity of the complement in 1 MHD, and the less sensitive will be the hæmolytic system. A 5 per cent suspension provides a less sensitive system than a 3 per cent suspension. The density is checked and adjusted if necessary colorometrically (Wyller, 1929; Greval, 1929; Greval, Yesudian and Choudhury, 1930). An unadjusted suspension is quite capable of turning a = reaction into a - reaction and *vice versa*. The error resulting from lack of attention to this point, though significant, is not so serious as those resulting from lack of attention to the complement and the antigen.

The human serum has a natural hæmolytic amboceptor against sheep's red cells. This fact engaged the attention of serologists about twenty years ago. It was feared that some positive human sera might turn negative falsely because of an excess of this amboceptor. Two safeguards were provided: (i) the amboceptor was absorbed or (ii) human red cell suspension was used. The first safeguard was unnecessary (Greval, 1927), and the second not only provided an inferior hæmolytic system (because of the low titre of the human-rabbit hæmolytic amboceptor) but actually introduced more problems (because of the groups and types) than it solved.

5. *The writer's scheme of a complement fixation test for syphilis.*—

(1) *For serum.*—Five tubes are used as follows:—

	1st tube (serum control)	2nd tube (for +)	3rd tube (also for +)	4th tube (for ++)	5th tube (for +++)
Antigen ..	<i>nil</i>	Cholesterinized Bordet.	McIntosh and Fildes	McIntosh and Fildes	Plain alcoholic heart extract.
Complement ..	2 MHD	2 MHD	3 MHD	5 MHD	4 MHD

The procedure of preparing the antigens has been given in detail previously (Greval, Chandra and Das, *loc. cit.*).

Very briefly, in the test proper, with a 1 in 5 dilution of the unknown sera, (i) the plain alcoholic heart extract reacts with strongly positive sera only, designated +++; (ii) the cholesterinized alcoholic heart extract reacts with moderate positive and weakly positive sera, designated ++ and + respectively according to the dose of the complement fixed; (iii) Bordet's antigen is more sensitive but less

A sixth tube is put up for clinically known cases only. It contains phenolized McIntosh and Fildes' antigen and complement 3 MHD.

For reasons of economy, the test may be split up into two parts: 4th, 5th and 6th tubes are put up only when the 2nd and 3rd tubes show inhibition of lysis of a high degree (+ or a trace of lysis only, designated T).

The results are based on McIntosh and Fildes' antigen and alcoholic heart extract. Cholesterinized Bordet's antigen and phenolized McIntosh and Fildes' antigen, if giving a + reaction,

merely draw attention to a doubtful result or even a negative result with a significant history.

The results are recorded (after the tubes have been in a refrigerator, or at ice-box temperature, overnight, to make sure of traces of hæmolysis) and reported as follows :—

Tubes :—					Report
1	2	3	4	5	
—	—	—	—	—	— Negative.
—	+	+	+	+	+++ Strongly positive.
—	+	+	+	+	++ Positive.
—	+	+	±/—	—	+ Weakly positive.
—	+	T	T	—	± Doubtful. Such reactions are not 9/10 to 5/10 positive.
—	+	±	±	—	± Doubtful. Repeated before reporting.
—	+	?—	—	—	± Doubtful with significant history.
—	+	—	—	—	— Negative without significant history.
—	T/±	—	—	—	— Negative.
—	—	T/±	±	—	± Doubtful. A + in tubes 3 and 4 should be retested. T is the likely reaction. A persisting + is duly reported positive.

It will be observed that tube 2 does not count when the plus or minus sign is recorded.

Doubtful reactions or even negative reactions with significant histories are further tested with (i) half the dose of the sera and (ii) half the dose of the antigen (only McIntosh and Fildes') to exclude paradoxical reactions (less reaction with more reagent).

(2) *For cerebrospinal fluid.*—Cerebrospinal fluid, without inactivation, is also put up with the three antigens in two strengths : (i) undiluted fluid, and (ii) two volumes of undiluted fluid instead of one volume. The 5 MHD tube is omitted. Inhibition of lysis in the tube containing two volumes of the undiluted cerebrospinal fluid, even when complete, is not accepted as a positive reaction unless there is also a definite inhibition of lysis in the tube containing one volume of undiluted fluid. The results are recorded and reported as follows :—

+++ Strongly positive, when complete inhibition of lysis occurs with the alcoholic heart extract in one or both tubes, subject to the provision concerning two volumes.

++ Positive, when complete inhibition occurs with the McIntosh and Fildes' antigen in both tubes.

+ Weakly positive, when inhibition is complete with the McIntosh and Fildes' antigen with 2 volumes of the fluid and partial but well marked with 1 volume.

± Doubtful, when partial but well-marked inhibition occurs in one or both tubes with McIntosh and Fildes' antigen.

— Negative, when no inhibition or inhibition of a poor quality occurs with the McIntosh and Fildes' antigen.

The tube put up with Bordet's cholesterinized antigen supports the inhibition of lysis in the corresponding tube put up with the McIntosh and Fildes' antigen.

Paradoxical reactions are excluded.

6. *A complement fixation test for syphilis done with several antigens versus several tests for syphilis.*—The writer suggested in 1939 (Greval, Chandra and Das, *loc. cit.*) that a Wassermann reaction done with several antigens should be preferred to several different reactions done for syphilis. When all is said and done, the flocculation tests have not succeeded in taking the place of the Wassermann reaction. Harrison (1931) 'would not found a diagnosis on a serum test unless the Wassermann reaction was positive'. This statement represents the opinion of most workers even after the issue of the League of Nations' Health Organization Report of the Second Laboratory Conference on the Sero-diagnosis of Syphilis (1928), resolution I of which states regarding the flocculation-tests that 'the conference . . . is of opinion that the best of them may be regarded as equal in value to the best of those which depend on fixation of complement (Bordet-Wassermann)'.

II. The false reactions

False positive reactions.—The following conditions have been held responsible for a false-positive reaction (Smith, 1940) :—

1. Other diseases—leprosy, yaws, malaria, trypanosomiasis, pinta and bejal frequently; septicæmia, endocarditis, pneumonia, tuberculosis, relapsing fever, spotted fever, typhus fever, scarlet fever, infectious mononucleosis, pernicious anæmia, leukæmia, xanthomatosis, severe jaundice and lymphopathia venereum less frequently; others very infrequently.

2. Bacterial growth in serum.

3. Excess of fat and digestive products in serum.

4. Passive transfer from the mother.

5. High barometric pressure increases tendency.

6. Improperly prepared titrated and mixed reagents.

7. Probably some "cured" cases of syphilis.

Item 6 may be eliminated. It has no place in a standardized and controlled technique.

Attention is drawn to three other conditions : kala-azar (Greval, Sen Gupta and Napier, 1939), lecithinophile eosinophilia (Greval, 1940), and the lecithinophile hepato-gastro-intestinal syndrome (Greval and Sen, 1942).

False negative reactions.—Weak or even negative reactions of the blood in early and late syphilis are well known. What is not so well known is that 'for no apparent cause the bloods of thirty per cent of the patients slowly revert to negative, even though they may show definite signs of syphilis during this period' (Becker, 1937); hence the specially sensitive antigens used for clinically known cases. Even an error on the right side resulting in such cases

being reported 'doubtful' or even 'weakly positive' will suggest to the clinician the need for a thorough examination of the nervous and the cardiovascular system. As a matter of fact 'it is in these cases that persistently weakly positive reactions are found' (Becker).

The writer does not favour a provocative injection which is as likely to accentuate a false reaction as a true one. History, clinical scrutiny, and repetition of the reaction after the subsidence of a passing morbid state are more likely to help. 'One positive test will usually convict a labourer over his denial; two may indict a railroad president or a banker; but I have known three to be insufficient to satisfy a clinician of the "guilt" of a minister' (Becker).

III. Wassermann positive rate for Indians

The writer's figures, much lower than those of previous workers, are as follows (Greval and Sen, *loc. cit.*) :—

Crude rate (found initially) .. 8.7 per cent.

Corrected rate (persisting finally,
without anti-syphilitic treatment) .. 5.3 per cent.

The true latent syphilis rate must be below 5.3 per cent in towns like Calcutta. In the country it must be much lower.

IV. A new name for the Wassermann reaction, Lecithin Complement Fixation (LCF).

The original technique of the reaction was materially different from the present techniques. It depended upon the use of a *restricted quantity of the hæmolytic amboceptor* and an *excess of the complement*: it was a *qualitative test*. The present-day techniques of most workers in England and America depend upon the use of an *excess of the amboceptor* and a *restricted quantity of the complement*: they provide a *quantitative test*. In America the reaction has been re-named after the serologists who have introduced the modification. The writer suggested in 1940 (Greval, Chandra and Das, *loc. cit.*) that it should be re-named Lecithin Complement Fixation (LCF). The name would be particularly useful in the tropics (and elsewhere too in cases with tropical histories) in allaying the alarm caused by doubtful, '50 to 90 per cent positive' and even positive Wassermann reaction. Diseases other than syphilis can undoubtedly be responsible for the reaction in the tropics.

The active substance in the antigen is presumed to be chiefly lecithin. It may be another allied lipid, or it may consist of several lipoids. The letter L will represent any of these substances, if necessary.

Summary

1. *Certain features of the technique.*—Titrated positive controls are the only indicators of the day-to-day constancy and comparability of the reaction. The complement has six qualities, four of which make special adjustment

with the antigen necessary. The antigen must be standardized with the aid of the titrated controls. The red cell suspension must also be standardized. In the writer's scheme, three antigens are used routinely and four in known cases, and the dose of the antigen and the serum is halved under certain conditions. Complement-fixation tests for syphilis done with several antigens should be preferred to several different tests for syphilis.

2. *The false reactions.*—To the usual list of conditions responsible for false positive reaction should be added (i) kala-azar, (ii) lecithinophile eosinophilia, and (iii) the lecithinophile hepatogastro-intestinal syndrome. Quite a large percentage of positive cases while still suffering from syphilis turn negative without treatment. Provocative injection is not recommended. Clinical scrutiny and repetition of the doubtful reactions are recommended.

3. Wassermann positive rate for Indians.—

(i) Crude rate (found initially) 8.7 per cent and (ii) corrected rate (persisting finally, without anti-syphilitic treatment) 5.3 per cent. The true latent syphilis rate must be below 5.3 per cent in towns and much lower in the country.

4. *A new name for the reaction.*—The present day Wassermann reaction is so different from the original reaction that it might as well be re-named Lecithin Complement Fixation (LCF). This name would indicate its basis and also allay alarm in cases with tropical histories.

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A MASSIVE ANEURYSM OF THE INNOMINATE ARTERY. A CASE WITH FATAL TERMINATION FROM SLOW 'EXTERNAL RUPTURE'

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THE following case report illustrates the devastating effects of massive aneurysms arising from the innominate artery; in this particular case, an aneurysm of this type, after attaining gigantic proportions (probably the largest aneurysm of the innominate artery on record), caused death, from slow external rupture, the so-called weeping of an aneurysm.

The patient, a Muslim male, aged 50, unemployed, was admitted into the K. E. M. Hospital, Bombay, on 14th August, 1942, complaining of a painful swelling in the right side of the neck. There was an old history of primary chancre, about thirty years ago; a year or two after the development of the primary sore, there had been a generalized skin rash, with sore throat, adenitis and malaise. He had had from time to time attacks of pains in the joints.

In June 1942, he observed for the first time a sort of vague or ill-defined pain in the neck and upper part of the chest, on the right side; paroxysmal to begin with, this pain had become continuous and intractable since July 1942. Two months before admission, the patient had noticed the appearance of a small



Fig. 1.

'boil-like' swelling in the lower part of the neck, on the right side, above the line of the clavicle; this had shown a slow and progressive increase in size until the day of admission.

On examination, the patient, a well-developed and well-nourished male of about fifty, was found to have a tumour or lump, the size of an orange, in the region of the right sterno-clavicular joint. It was about 3 to 4 inches in diameter and exhibited expansile pulsation, a systolic thrill and a systolic murmur. The patient, who was rather short of breath, preferred to adopt the semi-sitting position. The blood pressure was 130 mm. Hg. systolic and about 70 diastolic. The blood Kahn was 'three-plus'. Fluoroscopy revealed a 'normal aortic arch' with a large aneurysmal swelling on the right side corresponding to the position of

the innominate artery; the trachea was slightly displaced to the left side.

For a month after admission, the general condition of the patient remained stationary in spite of the lump showing a progressive increase in size; after that he showed progressively increasing dyspnoea; great respiratory distress and complained bitterly of pain, intense and agonizing, in the region of the aneurysm and along the right upper extremity. In spite of medical treatment, in the form of rest in bed, a restricted diet and the administration of anti-syphilitic drugs, his condition deteriorated rather rapidly.

When re-examined on 3rd December, 1942, the patient was found sitting up in bed, obviously in great distress. There was a large swelling, larger than a football and over 10 inches in diameter, over the neck and the upper part of the chest; the skin over it was tense, glossy and red, with a tendency to ulcerate in parts; expansile pulsation was not only palpable but also visible; a systolic thrill could readily be felt over the swelling, while a loud and long systolic murmur was also audible. The face of the patient was congested



Fig. 2.

and had a cyanotic hue, the neck veins were markedly engorged, and small venules were clearly visible within the skin overlying the aneurysmal swelling. Radial pulsations appeared to be equal on the two sides though the right pupil was larger than the left; the trachea was displaced slightly to the left. The apex-beat was visible and palpable in the 5th space, 5½ inches from the midline. Both heart-sounds appeared indistinct or muffled in the region of the apex; there was a tendency to reduplication of the second sound in the basal areas of the heart.

During the first two weeks of December, there was a noticeable and rapid deterioration in health of the patient in spite of medical treatment; in spite of repeated heroic doses of morphia, the patient was restless and in pain. On the 15th December, blood was seen to ooze out from one of the ulcerated patches of skin over the centre of the lump; this oozing of blood continued for three whole days and then the patient died after having lost several pints of blood in this manner. An autopsy was, unfortunately, not permitted by the relatives of the patient.

Discussion

Aneurysms of the innominate artery, on account of their striking character and progressive course, have for centuries attracted the attention of clinicians. In spite of the great clinical interest that these aneurysms have

aroused, one must admit their relative infrequency; they are said to account for only about 3 per cent of all internal aneurysms (Osler, 1908; Reid and Andrus, 1931). According to Olsler, Antyllus, a surgeon living in the second century A.D., was the first clinician to refer to the existence of innominate aneurysms. Valsalva, the famous Italian physician of the eighteenth century, has been credited with having cured several cases of arterial aneurysms (including one case of innominate aneurysm) by the simple expedient of under-feeding and over-resting his patients.

Much has been written in medical literature about the symptomatology and diagnosis of these aneurysms of the innominate artery. Their most striking characteristics are: (1) the initial symptom complained of is usually pain in the right shoulder, (2) the most conspicuous presenting sign of these aneurysms is usually the presence of a pulsating tumour in the neck, (3) symptoms and signs of compression, e.g. from pressure on structures such as the larynx and trachea, are much less frequent in cases of innominate aneurysm than in cases of aortic aneurysm, and (4) the direction of spread of innominate aneurysms is variable, depending on the lines of least resistance; most often they spread upwards, under the sternomastoid, into the neck.

Piersol (1912) has given a list of clinical features of importance in the diagnosis of innominate aneurysm, viz, (1) weakness of the radial or carotid pulse on the right side, (2) venous congestion of the face, (3) cough, hoarseness or aphonia, (4) dilatation of pupils, (5) cough from pressure on the phrenic nerve, (6) pains in the right arm, head and neck, from pressure on the brachial or cervical plexuses, (7) dyspnoea and dysphagia, and (8) obliteration of the supra-sternal depression with bulging at or above the right sterno-clavicular articulation.

The subject of roentgenology, as applied to the diagnosis of aneurysms of the innominate artery, has been reviewed extensively by various observers. Williams (1903) was probably the first man to have diagnosed innominate aneurysm on the basis of a radiological examination, in 1897.

The outlook in these cases of innominate aneurysm is certainly very poor. There is a tendency for these aneurysms to rupture, either externally (as in the present case) or internally into the trachea, bronchus, oesophagus, pleural cavity or pericardial sac.

Medical treatment consists in (1) starving or under-feeding the patient, (2) keeping the patient at rest in bed, and (3) in trying anti-syphilitic remedies. Surgical procedures, which have been advocated from time to time and which have proved successful in a certain percentage of cases, are: (1) the ligation of the right common carotid artery and the right subclavian artery, (2) the ligation of the right innominate

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SOME OBSERVATIONS ON BRAHMACHARI'S DISEASE (POST-KALA-AZAR INFECTION OF THE SKIN WITH *LEISHMANIA DONOVANI*)

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In a previous paper (1942) on post-kala-azar infection of the skin with *Leishmania donovani* I suggested that the proper name of the disease should be Brahmachari's disease to be named after the discoverer, or dermal leishmanoid as it was originally designated by him.

The chronicity of the disease

Its chronicity may extend over several years. Muir (1930) described the case of a patient who suffered from the disease for 35 years. Napier mentions a case who had been treated for 30 years as a leper.

The following notes describe the history and lesions of a case over a long period of more than 11 years:—

The patient, aged 22 years, had an attack of kala-azar in 1919 and was treated with sodium antimonyl tartrate (18 injections in all being given) after which he was apparently cured. Two years after completion of treatment for kala-azar, the patient began to notice

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artery and vein, (3) the use of Reid's (1926) technique of inducing clot-formation within the aneurysmal sac by electrical means, (4) the injection of quinine hydrochloride and ethyl carbamate, and (5) Babcock's (1932) operation of inducing an artificial fistula between the common carotid artery and the internal jugular vein.

Summary

The present case report deals with a massive aneurysm of the innominate artery (probably the largest innominate aneurysm on record) arising in a syphilitic male and terminating fatally from slow external rupture after a course of four months.

My thanks are due to Dr. A. Hameed, M.D., and to the Dean of the K. E. M. Hospital, Bombay, for permission to publish this unusual case report.

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erythematous patches on the skin of his body with small round reddish papules. In some places bigger patches were found. After some time whitish patches appeared on arms and legs and part of the chest.

The appearance of the skin lesions in July 1922 when the patient came for treatment for the first time, and in 1933, i.e. 11 years later, when he came again for their treatment is described below :—

Skin lesions in July 1922

Face—Somewhat erythematous. There is a nodule over the chin.

Arm and forearm—Large areas of depigmentation.

Axillae—Depigmented patches.

Neck and upper part of the chest—Depigmented patches.

Thigh—Depigmented patches with a few reddish nodules.

Knees—Depigmented patches on the skin, especially of the right knee.

Palms of hands—Normal.

Lesions seen in 1933

Erythema almost absent. No nodule on the chin. Small streaks of erythema on the cheeks and forehead.

Depigmentation almost absent and replaced by small reddish patches consisting of conglomerated small reddish papules.

Red papules conglomerated with each other.

No depigmentation but there is presence of reddish patches.

No depigmentation. Streaks of erythema.

Large reddish nodules on the skin.

Patches of depigmentation

The sequence of the changes of the appearance of the skin lesions may be summarized as follows :—

(1) Erythema, (2) depigmentation, (3) small reddish patches some of which consist of coalesced red papules, and (4) appearance of red nodules on the knees.

In the palm of the hands, there were patches of depigmentation in 1933 which were not present in 1922.

The evolution of the successive phases of the skin lesions in the course of several years has not been recorded before, as far as I am aware.

The relation of the disease to kala-azar

In this connection it is worth while to quote here from a paper of Napier and Krishnan (1933) who studied the relative incidence of dermal leishmaniasis and kala-azar in Bengal.

'In this area the population was about 5,000; the kala-azar incidence was 378 and the dermal leishmaniasis incidence 10, over a period of six years. By systematic examination of 120 persons who had had kala-azar, 6 were found to have dermal lesions. If we take the first figures we see that the proportion of dermal to visceral cases was 1 to 20.'

On the other hand, they found that the proportion of dermal to visceral cases in the village of Kayalpatnam, Madras, was not less than 1 to 9, and therefore in this village the dermal lesions are more common than they are in Bengal.

They concluded that the incidence of post-kala-azar dermal leishmaniasis is in direct proportion to the chronicity of the leishmania infection in the population in any locality, and

that 'the proportion of dermal cases to visceral cases is higher in Madras than in either Bengal or Assam. Our conclusion is that in Southern India are the oldest foci of kala-azar as far as India is concerned, that here the disease has passed through the two stages now seen to exist in Assam and Bengal, respectively, and has reached a "chronic" stage where there is not rise and fall in incidence from year to year and the disease is truly endemic, and that the transmission is almost entirely from dermal infections, so that treatment of kala-azar cases alone does not affect the general incidence of the disease'.

The theory that the incidence of post-kala-azar dermal lesions in any locality is directly related to the antiquity of kala-azar in that locality is open to criticism. It has been pointed by Knowles (1934) : 'It now seems almost possible to trace the previous history of kala-azar in India in retrospect. The disease was probably first introduced into Madras (probably from China) in the days prior to the British occupation of India. From there it probably spread slowly over most of the present Madras Presidency.' If this statement is accurate the antiquity of kala-azar in China is much greater than in Madras and one would expect that cases of post-kala-azar dermal lesions would be much greater in China than in Madras. But as a matter of fact, in practice however very few cases of post-kala-azar dermal leishmaniasis have been reported from China. Yao and Jung Sun (1936) in their paper on the occurrence of dermal leishmaniasis in China wrote as follows : 'Both of us have made careful search among the treated cases either from clinics or in the out-patient department of our Kala-azar Research Station, Tsing-Kiang-pu, China. So far we have found only 3 cases which showed early depigmented areas practically all over the body, about one year after treatment'.

The possibility of the disease being a factor in the transmission of antimony-fast leishmania from man to man

In the existence of post-kala-azar dermal lesions, one is faced with the fact that some cases of this disease may be carriers of antimony-fast parasites : if these parasites infect a fresh host, it may be presumed that the disease may manifest itself as an antimony-resistant visceral leishmaniasis, and if this happens, the treatment of such cases with antimony may be a very difficult problem. It is not however possible to state whether antimony-resistant cases of kala-azar are really increasing in any locality or not in the present state of our knowledge.

Let us consider the types of post-kala-azar dermal lesions that may be met with :—

(1) Cases yielding to antimonial treatment like an ordinary case of kala-azar, (2) cases yielding to antimonial treatment, but only after long treatment, (3) cases that are resistant and require a very prolonged course of treatment,

and (4) some cases that appear to be absolutely resistant.

The last two types might give rise to antimony-fast visceral leishmaniasis, which may be a menace to the affected locality.

Certain observers have opined that in Assam, where the infection of kala-azar is transmitted from visceral cases, there is a tendency for the transferred infection to assume a visceral form, whereas in Bengal with the appearance of dermal lesions an increasing number of transmissions occur from dermal cases and there is a gradual tendency on the part of the parasite to assume a dermal localization.

All these points require further investigation.

Napier and Krishnan (1931) have held that the visceral localization of the leishmania in kala-azar is relatively unfavourable to the existence of the parasite, while their dermal localization is more favourable. Why then, it may be asked, do the parasites go to the internal organs at all, instead of living in the skin? Why does *Leishmania tropica* prefer to live in the skin instead of attacking the internal organs of the infected individual as *Leishmania donovani* does*? As already stated by me (1942) sometimes very few or no leishmania are found in the most extensive depigmented patches of dermal leishmaniasis and the number of leishmaniae present in a nodule or papule is not always proportional to the degree of nodule or papule formation. The skin cannot therefore be regarded under ordinary conditions as being the most favourable site for their growth.

We may conceive that the surviving parasites shelter in the skin after those in the viscera have been destroyed by the immune bodies. The skin lesions may indicate a last stand in their struggle for existence against the defensive mechanism of the host who has been cured either spontaneously or after successful antimonial treatment. As I have previously suggested (1942), during the specific treatment of kala-azar the leishmania may be carried to the skin by the cells of the reticulo-endothelial system and also by other leucocytes. There in the skin the specific treatment may not reach the parasites in sufficient amount, and so the parasites may grow inside the leishmania-protective cells and subsequently give rise to the development of post-kala-azar dermal lesions.

This does not always hold, as many cases of Brahmachari's disease get cured by antimonial

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* These two sentences require some comment.

Surely parasites are not able to choose the tissues in which they live. *L. tropica* affects the skin either because it is unable to spread or is prevented from spreading more widely, or else because when it does so, it is rapidly killed off. *L. donovani* can and does spread widely, causing visceral leishmaniasis, during which phase skin lesions are slight or absent. With antimony treatment the visceral parasites are killed off, but in some cases parasites persist in the skin where they may produce lesions.—EDITOR.

ACUTE ASEPTIC MENINGITIS

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WHILE treating cases of meningitis one often sees some patients who cannot be grouped under any specific type of meningitis though symptoms and signs may be typical of the disease, e.g. headache, fever, head retraction, Kernig's sign, etc. But the cerebro-spinal fluid shows slight changes on chemical, microscopical and cultural examinations. To such cases the term acute aseptic meningitis or benign lymphocytic meningitis has been given. Wallgren (1925) gave the first account of this condition. His observations were based on a small epidemic. Since then it has been described from time to time by many physicians under different names—aseptic benign purulent meningitis (Schiff, 1930), idiopathic benign serous meningitis (Andersen and Wulff, 1930), epidemic meningitis serosa (Epstein and Dameshek, 1931), simple meningitis (Abraham, Rowland, etc.), benign lymphocytic chorio-meningitis (Armstrong and Lillie, 1934).

The multiplicity of names is due to the fact that the aetiology of the disease is not fully understood and the pathological changes were variable. Of all the above names, acute aseptic meningitis and benign lymphocytic meningitis are the ones now widely used. It is caused by a filtrable virus (Armstrong and Lillie, 1934) similar to that of encephalitis lethargica. Some (Andersen and Wulff) believe that the same virus may give rise to both the diseases, the manifestations depending upon the intensity and the site of affection; when the brain itself is the site of involvement, it causes acute encephalitis lethargica, whereas when the meninges are involved, acute aseptic meningitis results. Some workers have stressed its relationship to acute anterior poliomyelitis (Rish and Rowland).

Three viruses have been isolated by different workers from cases having a similar clinical picture—(i) the virus of lymphocytic chorio-meningitis (in U.S. America, Great Britain, France and Japan), (ii) the virus of swine

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treatment. Is it possible that some of the parasites in the skin become antimony-fast?

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herd's disease (in France, Switzerland and Italy), and (iii) the virus of pseudo-lymphocytic chorio-meningitis (in England). The viruses of American and European sources have been found to be identical. These viruses have been isolated in only a small number of cases of acute aseptic meningitis. Of others the ætiology is still unknown.

It has not yet been definitely established what is the source of infection and how the virus enters the human body. The virus may exist in healthy mice, and the latter may act as carriers of the disease. It is possible that it gets into the human body through the skin or by the nasal route. It has also been suggested that the dog may transmit the disease to man.

Pathology

Pathological changes cannot be definitely described as only a few autopsies have been performed and in them there have been variations in the findings. The meninges show an inflammatory reaction. They are cedematous and infiltrated with lymphocytes and endothelial cells. The brain is injected and shows widespread encephalitic changes. On microscopic examination there is perivascular 'cuffing' and infiltration by lymphocytes. The ventricles and choroid plexus also show an inflammatory reaction.

Symptoms and signs

The patient suffering from this disease may be a child or an adult but usually is below 20 years. The onset is acute but it may be preceded by sore throat. Headache is marked (may be frontal or occipital) with continuous fever and insomnia, stiff neck or head retraction, positive Kernig's sign; reflexes may be sluggish or brisk. The sensations usually remain unaffected and this is very characteristic. Though convulsions and lethargic symptoms may appear, the mental condition remains clear and the patient is bright.

In some cases the cranial nerves may be involved. There may be a suggestion of nystagmus but true nystagmus is not found. Photophobia and papilloedema may be present, the latter indicating sudden onset of increased intra-cranial tension.

Other symptoms have also been occasionally noticed, e.g. vomiting and abdominal pain, delirium, stupor, frequent and painful micturition, diarrhoea or constipation. In a few cases, paralytic symptoms of some part of the body have also been noticed, e.g. of the face, palate, eyelids and legs, and in others involuntary movements and some disturbances of sensation, e.g. pins and needles, have also been observed.

There are no changes in other systems excepting the blood which may show some polymorphonuclear leucocytosis.

On lumbar puncture the cerebro-spinal fluid is found to be under pressure. It is usually clear; in some cases, a cob-web like clot may form on standing; it may be opalescent or

actually purulent during the first two or three days. The chlorides and sugar may be normal or only slightly reduced; proteins may be little above the normal. The cell count is increased—usually the lymphocytes—but in some cases polymorphonuclear cells predominate especially in the early stages of the disease. Culture is always sterile. The Wassermann reaction of the cerebro-spinal fluid is always negative, and colloidal gold reactions give the meningitis type of curve.

The course of the disease is usually uneventful, and recovery is the rule. The duration of the disease is about 1 to 3 weeks. No complications and sequelæ have been observed.

Diagnosis and differential diagnosis

The chief features which help in the diagnosis are :—

1. Acute onset with meningitis symptoms.
2. Meningeal changes in the cerebro-spinal fluid. Increase of cells with normal or only slight increase of proteins, normal or only slight diminution of chlorides and sugar.
3. Short benign course without sequelæ.
4. No epidemiological relation to any known infectious meningeal disease.
5. No local infections such as otitis media or sinusitis.
6. No mental stupor. The patient is mentally alert.
7. Blood sedimentation rate is normal.

The differential diagnosis has to be made from :—

1. Tuberculous meningitis: The onset in tuberculous meningitis is insidious. The patient is dull and lethargic. The fall in the chlorides in the cerebro-spinal fluid takes some time, and the protein rises higher than in acute aseptic meningitis. Glucose is diminished and tubercle bacilli are found on microscopic examination. The tryptophane reaction is positive in the cerebro-spinal fluid. The blood sedimentation rate is increased. At the end of the 7th day, tuberculous meningitis gets worse while one of aseptic meningitis gets better. A case of tuberculous meningitis ends fatally.

2. Encephalitis lethargica may be difficult to differentiate, as the cerebro-spinal fluid findings may be quite similar in the two diseases, but the patients of acute encephalitis lethargica are dull and lethargic and never bright. Sequelæ are also common in acute encephalitis lethargica.

Acute anterior poliomyelitis can be diagnosed from acute aseptic meningitis by the presence of muscular weakness and absence of reflexes.

Meningism, serous meningitis, spirochætal meningitis due to leptospira icterohæmorrhagæ, syphilitic meningitis and meningitis occurring in mumps and herpes zoster can be diagnosed by the associated symptoms of these conditions and by the examination of the cerebro-spinal fluid.

Glandular fever when associated with meningeal symptoms shows lymphocytosis in the

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ADMINISTERING DRUGS TO RODENTS BY MOUTH

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DIFFICULTY is often experienced in administering drugs in definite amounts to guinea-pigs, rats, etc., by mouth. Drugs may be mixed with

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cerebro-spinal fluid; there is glandular enlargement.

Prognosis

The disease always takes a favourable course and ends in recovery.

Treatment

The treatment is usually symptomatic. Lumbar puncture relieves the tension of the cerebro-spinal fluid and thereby the headache.

Case reports

Case 1.—K. D., aged 12 years, was admitted on 6th April, 1942, with a history of fever for two days, vomiting on eight occasions and delirium for a day. On examination, there was rigidity of the neck; Kernig's sign was positive and pupils were reacting sluggishly to light; cerebro-spinal fluid was clear but under tension, chlorides 570 mgm. per cent, sugar 60 mgm. per cent, albumin in traces, 20 cells per c.mm.; culture was sterile. The patient improved under treatment and was taken away by her relatives on 9th April in a much improved condition.

Case 2.—M. S., aged 6 years, admitted on 12th January, 1943, with a history of fever and rigidity of the neck. The rigidity of neck appeared on the second day of fever. On examination, the patient was conscious but a little restless, pupils were contracted, rigidity of the neck was present and Kernig's sign was positive. The cerebro-spinal fluid was under tension and was opalescent; chlorides 600 mgm. per cent, sugar present, albumin in traces, pus cells present, culture was sterile. The cerebro-spinal fluid was again examined two days later on the 14th. Pus cells were absent, cell count 18 per c.mm. The patient rapidly improved and was discharged on 19th January, 1943, as cured.

During the period of 18 months, 36 cases showing symptoms of meningitis were admitted into the Thomason Hospital, Agra. Of these 22 were meningococcal, 4 pneumococcal, 4 tuberculous, 3 associated with encephalitis lethargica and 3 of acute aseptic meningitis.

I wish to thank Major-General H. C. Buckley, I.M.S., Superintendent of the Thomason Hospital, for permission to report the above cases. I am also thankful to Dr. G. N. Vyas, Professor of Medicine, for permission to report one of his cases (case no. 2).

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food and given to them, but it is very difficult to be sure of the exact quantity taken by the animal. Sometimes drugs in measured amounts are introduced into the oesophagus or the stomach with the help of a rubber catheter, but during the process of introducing the catheter, specially in smaller animals such as guinea-pigs, rats, etc., the catheter may be pushed by the tongue in between the upper and lower set of teeth and may be bitten and punctured by them and the fluid comes out through the punctures. It is therefore very difficult to be sure just how much of the drug reaches the stomach.

Rodents have two long central incisors in each jaw. They have no canine teeth. The other teeth are placed inside the oral cavity and there is a large space between the incisors and the other teeth; this is why the other teeth are not visible when the mouth is opened. This is well demonstrated in the accompanying diagram (see figure 1).

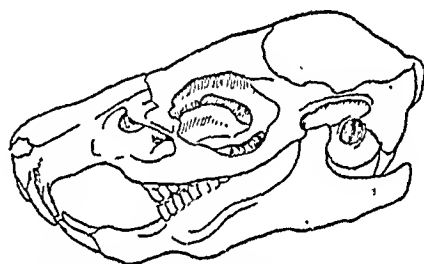


Fig. 1.—Diagram showing the arrangement of teeth and the gap between the incisors and other teeth.

A straight needle sufficiently long to reach the upper part of the oesophagus when introduced is used in this technique. It is usually $3\frac{1}{2}$ to 4 inches long when used for guinea-pigs. As described by us (Panja and Paul, 1943) its pointed end is made bulbous with lead and made smooth so that it does not injure the passages. The round distal end of the needle should be about 2 mm. in diameter. The proximal end should fit tightly either directly to a record syringe or indirectly by means of a rubber tube.

Technique.—The guinea-pig is kept fasting for at least 3 to 4 hours before feeding to ensure that the stomach is sufficiently empty to accommodate the fluid to be given. The empty stomach of a guinea-pig, 350 gms. in weight, can comfortably hold about 15 c.cm. of fluid.

The guinea-pig is held with head upwards by an assistant, the right hand holding the two hind legs and the left hand holding the two forelegs by the sides of its head and pushing the jaw upwards so that the head, neck and trunk are in a straight line.

The operator then opens the mouth of the guinea-pig from the side, pressing on the tongue by means of a pair of ordinary forceps with his left hand. The arms of the forceps are kept separated by means of a finger. At first the needle without the syringe is introduced into the mouth centrally, perpendicularly and slightly

backwards till it touches the back of the palate. Then gliding over the palate between it and the back of the tongue, the needle is pushed very lightly downwards, slightly backwards and to the right of the guinea-pig, at times slightly pressing on the tongue with its distal end. Thus the needle very easily and comfortably goes down the pharynx to the œsophagus. It should be noted that there is little chance of introducing the needle into the larynx or trachea as they lie in front and slightly to the left of the œsophagus. The animal usually coughs if the needle strikes the larynx or goes into it. In these cases it is better to take out the needle and try again. The needle should remain slightly obliquely, at the left of the upper central incisors at the top, and in the œsophagus on the right side of the neck below. This is well shown in the accompanying picture (see figure 2).



Fig. 2.—Picture showing the method of holding the animal, and the needle in position.

Sometimes the animals move very violently. In such cases it is better to wait till they are quiet.

Fluid is drawn inside the syringe to its required mark and the rest of the syringe is filled with air. It is then inverted, and any hanging drop at the tip is removed; otherwise the drop may flow outside down the needle to the larynx and cause coughing.

The syringe is now attached tightly to the needle. The piston is then pushed down very slowly, keeping pace with

respiration and deglutition. Sometimes fluid tends to regurgitate and cause coughing. This happens (a) when the needle does not go down into the œsophagus, (b) when the fluid is injected too quickly, or (c) when the animal holds its breath. In these cases it is best to wait till normal respiration is restored, then to push the needle further down, and inject the fluid slowly. If the animal is distressed with severe coughing, it is best to remove the needle, let the animal recover, and then start again. In rare instances the animals get shock, due to sudden over-distension of the stomach and consequent pressure on heart and lungs.

Before taking out the needle, the piston is pulled up, since any fluid in the needle might affect the larynx and induce coughing.

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THE ISOLYSINS

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THE intention is (i) to draw attention to the existence of isolysins (isohæmolysins) a and b as distinct from isonins (isohæmagglutinins) a and b, (ii) to give a complete serological constitution of blood groups inclusive of these antibodies, and (iii) to point out the danger of their presence in the donors' blood.

Isolysins a and b

The almost immediate hæmolysis occurring *in vitro* when incompatible bloods are mixed is due to the isolysins a and b, and is not merely a lytic effect produced by the powerful (high titre) isonins a and b. The isolysins are very closely associated with the isonins. The latter are usually, but not invariably, of high titre. Recently, the writers (Grevall, Bhattacharji and Roy Chowdhury, 1943) have given details of two isolysins which were not associated with isonins of high titre.

One of the isolysins was b in a subject O. It was associated with an isonin of a moderate titre (1 in 32). Further, the isonin b was of the same titre as the isonin a. The isolysin was strong. It lysed 2 per cent red cells B immediately, and red cells AB in a minute or so. It acted also in a dilution of 1 in 4 in saline. It could not be separated from the associated isonin.

Dilution of the lytic serum in saline when too weak to produce lysis prevented hæmagglutination until a weaker dilution was reached.

The serum could be inactivated by heat, and reactivated. Inactivation by aging was very slow. The reactivated serum could cause a delayed lysis.

The other isolysin was a, also in a subject O. It was much weaker and tended to be inactivated by age very rapidly. It was missed on

(Continued from previous column)

By this method a definite amount of the drug is introduced directly into the stomach of the animal.

My thanks are due to Dr. G. Panja, Officiating Professor of Pathology and Bacteriology, School of Tropical Medicine, Calcutta, for his kind help and guidance in the technique.

REFERENCE

PANJA, G., and PAUL, *Indian Med. Gaz.*, **78**, 190. B. M. (1943).

several occasions when the serum was tested twenty-four hours after the blood had been taken. It could also be reactivated.

The isolysins 'can even be demonstrated in the new born' (Halban, Jones quoted by Lattes, 1932) in whom isonins are usually weak and sometimes absent.

A complete serological constitution of blood groups, inclusive of isolysins

According to the hypothesis of Lattes (*loc. cit.*) the complete serological constitution of blood groups would be as follows:—

	Group O	Group A	Group B	Group AB
Isogen	O	A	B	AB
Isonin	ab	b	a	o
Isolysin	ab	b	a	o
Anti-isolysin (anti-iso-haemolysin).	o	anti-a	anti-b	anti-a and anti-b.

The strong isolysin b was used in detecting the presence of the supposed anti-isolysin b in the blood of four subjects B. Their red cells and sera were put up with an equal volume of the lytic serum in six ways: (i) 2 per cent suspension in saline, (ii) 2 per cent suspension in subjects' own serum, (iii) 2 per cent suspension in absorbed serum (absorbed previously with cells A), (iv) 2 per cent suspension in absorbed serum b, (v) 2 per cent suspension in absorbed serum ab (from subject O) and (vi) 2 per cent suspension in absorbed serum o (from subject AB).

The subjects' own serum delayed the lysis and thus protected the cells partly. Even human serum as such (from other groups) protected the cells partly. The protecting substance, however, was not more than could be expected to exist in the serum as a result of solution of isogens (iso-haemagglutinogens) A and B from the cells.

Lattes accepts this explanation of the isogens in solution for the neutralization of isonins a and b, but not for the neutralization of anti-isolysins a and b.

The majority of the isonin-containing sera (from all groups except AB) have no isolysins. The latter occur in only about 30 per cent of such sera (Wiener, 1935).

The danger of the presence of isolysin in donors' blood

The danger of the isolysin in the blood of an otherwise 'safe' universal donor for recipients A and B, and in donors A and B for recipients AB is obvious.

Weak isolysins may be missed if the serum is not tested the same day. Even such an

(Concluded at foot of next column)

PARKINSONIAN MANIFESTATIONS ARISING IN A PARSEE FAMILY WITH 'ESSENTIAL, PRIMARY OR FAMILIAL TREMOR'

By RUSTOM JAL VAKIL, M.D. (Lond.),
M.R.C.P. (Lond.), D.T.M. & H., F.R.F.P.S.G.
(King Edward Memorial Hospital, Bombay)

THE condition of 'primary', 'essential' or 'familial' tremor is familiar to most clinicians. It is a well-recognized and fairly common neurological entity with hereditary or familial trends, and is characterized by the appearance from birth or in early life of a 'fine' and rhythmic

(Continued from previous column)

apparently weak serum can cause delayed haemolysis with an excess of the complement.

Observations of workers on the 'accidents' caused by 'dangerous universal donors' have not made clear the causation of the accidents by the donors' plasma. At least two processes are concerned: (i) isohaemolysis and (ii) isohaemagglutination: the high titre isonins have been held responsible for both of them, in a general way. The rapid and complete haemolysis *in vitro*, from mixing of incompatible bloods, is definitely caused by isolysins alone. A slow and partial haemolysis from strong agglutination is known. Re-activated isolysins also cause delayed haemolysis.

Summary

1. A strong isolysin b and a weak isolysin a were found associated with isonins of moderate titre in two subjects O.

2. The strong isolysin b was used to test the presence of the anti-isolysins (according to Lattes' hypothesis) in four subjects B. None was found.

3. The danger of isolysins in the blood of otherwise 'safe' universal donor for recipients A and B and in the blood of donors A and B for recipients AB is obvious. The causation of the accidents of transfusion by the donors' plasma needs clarification. High titre isonins may not be solely responsible.

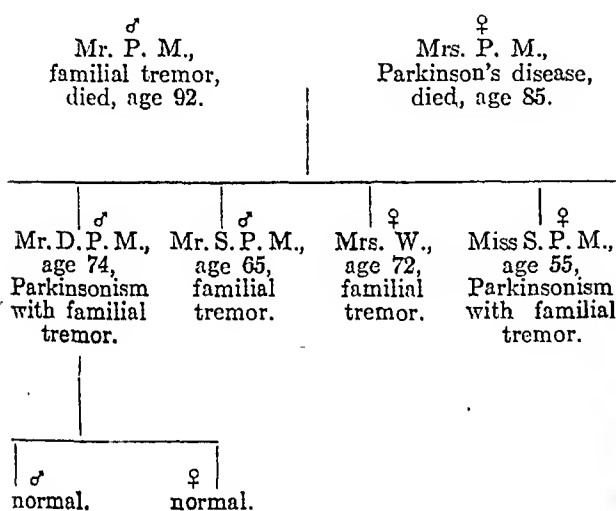
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- LATTES, L. (1932). *Individuality of the Blood in Biology and in Clinical and Forensic Medicine* (Translated by Berte), p. 74. Oxford University Press, London.
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tremor of 'small amplitude and without a characteristic tempo'.

Parkinson's disease is seldom if ever associated with this condition of 'familial tremor'; as far as I can ascertain, an association of this type has been reported in medical literature only twice. The present report deals with an unusual Parsee family of eight members (observed through three generations), in which five members suffer from the condition of 'familial' tremor, and as many as three members exhibit Parkinsonian characteristics. This unique family was brought to my notice recently by accident, when I was summoned to try and determine the cause of 'vertigo' in one of its members.

The accompanying diagram demonstrates at a glance the essential points of interest about this family.



It will be observed from the diagram that in the first generation reported, Mr. P. M. who is suffering from 'familial' tremors marries Mrs. P. M., a Parkinsonian. In the second generation consisting of four children, two members (one brother and one sister) have 'familial' tremors while the other two (one brother and one sister) exhibit Parkinsonian manifestations in addition to 'familial' tremors. In the third generation, there are only two members who are perfectly normal in all respects, and free from all tremors.

Familial tremor.—This was of an identical nature in all cases. It was a fine, rhythmic and rapid tremor observed in the distal portions of both upper extremities and in the lower lip; aggravated or accentuated by emotion, mental fatigue and by voluntary movements. The tremor had been observed in the affected members of the family from the age of infancy or childhood, and had persisted unchanged throughout life, without incapacitating them in any way.

Parkinsonism.—In the three members of the family affected by Parkinsonism, the tremor observed was of an entirely different nature. (Mrs. P. M., the mother, having died some years ago, has not been observed by me personally

but is believed to have displayed a full-blown picture of Parkinson's disease, coming on in middle life.) Having personally examined Mr. D. P. M. and Miss S. P. M., the two children with Parkinsonian manifestations, I am in a position to enumerate the main features of clinical interest:—(1) A *tremor*, very slow and coarse, displaying a 'fixed tempo', of the typical 'cigarette-rolling' or 'pill-rolling' type, bilaterally symmetrical and affecting the joints of the fingers, wrists and elbows. At the wrist, the tremors were highly complex, involving movements of flexion, extension pronation and supination. Also present were rotatory movements of both thumbs, tremors of the tongue, and opening and closing movements of the mouth from involvement of the mandibular muscles. Though accentuated by emotional factors, these tremors were practically unaffected by voluntary movements, and would disappear completely during sleep. They had been observed in both cases from the age of adolescence, and had displayed a tendency to increase slightly with age. (2) A certain amount of spasticity or rigidity of the 'cog-wheel' type was displayed by the muscle-groups of the upper extremities in both these cases. (3) The attitude of the body on standing was one of 'slight flexion' in both the cases; the gait, though characterized by short and slow steps, could not be described as 'shuffling' or 'festinating' in character.

Summary

This is probably the third time in medical literature that an association is recorded between the two neurological entities of Parkinsonism and 'familial, essential or primary tremor'. The present report deals with a unique family of eight members, with as many as five members exhibiting 'essential or primary' tremor and three with Parkinsonian manifestations, two of these three cases also showing 'familial tremor'.

EDITORIAL NOTE

Naga sore

Previously naga sore has been confined to more-or-less definite areas of India, chiefly Assam. In recent months, however, sores of a similar nature have been observed in people in parts of India not normally showing these sores. During recent months a large number of people have come to Calcutta in search of food, and few if any of them come from areas in which naga sore is normally found. Nevertheless among these people, very large numbers of sores have been seen which are indistinguishable from naga sore. We have received from Doctors D. Panja and L. M. Ghosh from the School of Tropical Medicine a paper on this subject, which will appear in our next issue. These sores are being seen in large numbers in various parts of India at the present time and this paper should be of considerable value.

A Mirror of Hospital Practice

A CASE OF TROPICAL EOSINOPHILIA ?*

By UPENDRA NATH CHAKRAVARTY, M.B.

Barisal

and

SUDHIR C. ROY, M.B.

Honorary Visiting Physician, Chest Department,
District Hospital, Barisal

A HINDU male, aged 29 years, complained of paroxysms of unproductive cough with asthmatic attacks occurring usually at night, low intermittent fever ranging between 97°F. and 100°F., urticaria, loss of appetite and loss of weight.

Present illness.—For a few days prior to the attack the patient felt exhausted and feverish towards the evenings. The appetite was lost, and there was loss of weight too. He attributed the symptoms to overwork and irregular hours.

One night as he was retiring to bed after unusually hard work, he was seized with a paroxysm of incessant cough. It was unproductive and there was marked wheezing and expiratory dyspnoea. He was restless and did not feel relieved in any position. The paroxysm lasted throughout the night and he was sleepless. The following morning the cough and dyspnoea ceased abruptly and he remained more or less free from symptoms during the day. The wheeze however persisted.

The paroxysms recurred every night usually after midnight, and he noticed intermittent rise of temperature, the maximum, 100°F., being reached at about 8 or 9 o'clock in the evening. About a week later there developed intense itching of the skin, and urticarial wheals appeared all over the body.

The duration of the illness was about three weeks.

Personal history.—There is nothing of any importance, except that for some time previous to the attack he had to work hard and was irregular in his habits especially with regard to meals. Moreover, he had been compelled to sleep in unsatisfactory hygienic surroundings.

Family history.—Recently the patient had been in contact with a sputum-negative case of pulmonary tuberculosis, but it was not intimate or close. The patient's father had had two attacks of hæmoptysis—one about 30 years back and the other about two years ago. There is nothing else of importance in the histories of other members of the family.

Past history.—Nine years ago the patient had an attack of dysentery, but the type was not definitely diagnosed. A year later he suffered from pharyngitis, and has since been suffering from occasional mild attacks, especially in winter.

Physical examination.—When first seen the patient was in the grip of what looked like an attack of severe bronchial asthma. The cough was incessant but unproductive. He was sitting up on the bed with hands outstretched gasping for breath. The wheeze was audible even at a distance.

On auscultation the usual signs of bronchial asthma were heard.

The temperature was raised to 100°F. The pulse was 95 per minute and full and bounding.

The spleen was not palpable but a suspicious 'thrust' was felt in the area on deep inspiration. There were no enlargement of lymph glands.

The liver was enlarged and could be felt about an inch below the costal margin; it was tender.

Course of management.—Bronchial asthma was diagnosed and 0.5 c.cm. of adrenalin chloride was at once injected subcutaneously. The patient was soon relieved and he expectorated a fair quantity of thick viscid sputum. Before adopting further anti-asthmatic routine

the patient was given a dose of anthelmintic. A previous stool examination had shown the presence of ascaris ova in large numbers.

The response to anti-asthmatic therapy was not satisfactory, the paroxysms of cough and dyspnoea were only partially controlled. Nevertheless, the treatment was continued for some more days, when suddenly there was a sharp rise of temperature with rigor. Aggravation of the paroxysms followed, and urticarial rashes were noticed for the first time at this stage.

Blood examination showed leucocytosis (22,000) with increase of eosinophils and polymorphonuclears (15 and 76 per cent respectively). No malaria parasites or microfilariae were found.

The anti-asthmatic regime was withheld and the patient was put on sulphapyridine in orthodox doses. The temperature subsided and the cough and dyspnoea appeared to be controlled after the first dose. On the second day the patient complained of painful and frequent micturition and the total quantity of urine in the whole day was greatly diminished. Sulphapyridine was accordingly discontinued and the anti-asthmatic regime was re-introduced, but it was followed by a relapse of the symptoms. On examination of the urine only traces of albumin and excess of phosphates were found. It was however noticed that the anti-asthmatic therapy did not produce any appreciable improvement in the patient's condition.

The blood was examined. Though the total leucocytic count had fallen slightly—the effect presumably of sulphapyridine—the eosinophils had increased to 25 per cent. A skiagram of the chest revealed prominent bronchial markings and heavy hilar shadows, but no infiltration.

One of us (U.N.C.) thought it to be a case of tropical eosinophilia, as described by various writers in India in recent years. The patient was put on intramuscular injections of calcium (Sandoz) mixed with redoxon and thiarisin (an organic arsenic compound). In addition ammonium chloride in 10 gr. doses and a sedative cough mixture were also prescribed. Further, the patient was advised to take salt-restricted diet.

During the first part of the treatment the total leucocytes and the eosinophils increased. There were no immature cells; on the contrary the eosinophils showed a marked shift to the right. Following the fourth injection the total white and the eosinophil counts registered a fall, and a simultaneous improvement of the patient's clinical symptoms was also noticed. The treatment was continued for some time more, and the patient made an uninterrupted recovery.

Blood counts

Date	Total WBC	DIFFERENTIAL COUNT : PER CENT			
		Poly.	Eosino.	Mono.	Lympho.
30-5-43	22,500	76	15	nil	9
4-6-43	20,500	60	25	nil	15
26-6-43	27,000	53	35	1	11
7-7-43	32,000	30	52	2	16
17-7-43	19,500	30	47	1	22
4-8-43	12,000	40	24	3	33

Total RBC throughout . . . between $4\frac{1}{2}$ to $5\frac{1}{2}$ millions

Discussion

The case reported by us was highly suggestive, and a provisional diagnosis of tropical eosinophilia was accordingly made. We have however noticed a few atypical features, for instance, the presence of urticaria and the absence of an enlargement of the spleen. The recentness of the disease may explain the peculiarities. Nevertheless, we believe that we have not erred

* Being a paper read at a Clinical Meeting of the Barisal Medical Union on 13th August, 1943.

in our diagnosis. At the same time we are aware that further investigations are necessary.

With regard to the interpretation of symptoms we have differed considerably from Weingarten. He has argued against an allergic state, and has based his contention, among others, on the high eosinophilia, the characteristic sign of the disease.

From our observations on this case we are drawn towards the view that tropical eosinophilia is an allergic phenomenon.

We wish to convey our thanks to Sj. Subodh Nath Roy Chowdhury for the laboratory help in this case.

A CASE OF PSEUDO-TUBERCULOSIS OF THE LUNGS WITH EOSINOPHILIA

By RASIKLAL L. SHAH, L.C.P.S.

Clinical Laboratory, Lallubhai Building, Rajkot

A HINDU male, aged 22 years, was seen by me on 27th January, 1943. He had fever for two days with slight cough and aching all over the body. Occasional wheezing sounds were audible in the lungs. The temperature was 100°F. One injection of quinine, 10 grains, along with a diaphoretic expectorant mixture was given.

Next day the temperature in the morning was 99°F. but in the evening it went up to 103°F. with severe rigors. Thinking it to be malaria, another quinine injection was given. On the third day in the morning the temperature was normal, but again in the evening it went up to 103°F. with severe rigors. A third injection of quinine was given to rule out the severe type of malarial fever.

At this stage his blood and urine were examined. The blood culture was negative after four days' incubation. Leucocytes 13,125 per c.mm., neutrophils 54 per cent, lymphocytes 26 per cent, monocytes 6 per cent, eosinophils 14 per cent. No parasites were found. Urine showed no abnormality.

Fever was more or less continuous, with congested throat suggestive of influenza. Injections of S.U.P. 36, 1 c.cm., were given successively on the 3rd, 4th, and 6th February. After the third injection the temperature was normal for six days, but again it went up every evening up to 100°F., till the 24th February when the patient had a sudden asthmatic attack. Râles and ronchi were audible all over the lungs, and the patient had severe dyspnoea. An injection of adrenophedrine was given with relief in a very short time.

Two days previous to this attack his blood and stool were examined. The Widal test was negative. Leucocytes 19,200 per c.mm., neutrophils 22 per cent, lymphocytes 16 per cent, monocytes 2 per cent, eosinophils 60 per cent. Stool report showed no abnormality.

A skiagram of the chest taken on the 18th February showed peribronchial infiltration. Two direct smears of sputum showed no acid-fast bacilli. The temperature gradually increased to 101°F. in the evening but was normal in the morning. Another blood count done on 14th March, 1943, showed a leucocytosis of 21,600 per c.mm. with 71 per cent eosinophils.

A reference to the literature led me to think that the patient might be suffering from pseudo-tuberculosis of the lungs with eosinophilia as described by Rudolf Treu (1943). Frimodt-Møller and Barton (1940) had however previously drawn attention to 'eosinophile lung' with a comparatively good prognosis although the skiagram simulated that of pulmonary tuberculosis of the miliary type.

Different doctors were consulted, and the case was investigated to exclude other possible causes. The patient was then put on acetylarsan injections as suggested by Rudolf Treu. He gradually improved and was quite well after 12 injections, though slight eosinophilia persisted. He was completely free from all the

symptoms. The temperature came to normal after seven injections, and the blood count on 10th March, after ten injections, showed total leucocytes 8,600 per c.mm., neutrophils 52 per cent, lymphocytes 28 per cent, monocytes 4 per cent, eosinophils 16 per cent.

The case presents two important features, viz, eosinophilic leucocytosis and pulmonary signs, with fever, cough and expectoration. Acetylarsan is worth a trial in such cases.

I am obliged to Dr. G. B. Mamkad for his guidance in writing this case report and for the references.

REFERENCES

- FRIMODT-MØLLER, C., and *Indian Med. Gaz.*, **75**, 607.
BARTON, R. M. (1940).
TREU, R. (1943) .. *Ibid.*, **78**, 70.

[Note.—Why quinine was given at all, why injections of quinine were used, and why blood examination for malaria parasites was done only after these injections is not clear.—EDITOR, *I. M. G.*]

A SYMPTOMLESS CASE OF RENAL CALCULUS IN BOTH KIDNEYS

By B. L. CHOPRA

Divisional Medical Officer, Ferozepore

A CLERK of this railway, 34 years of age, came about a month ago suffering from a cold abscess in the lumbar region—duration two months. He also had cough and evening temperature of 6 weeks' duration. The cold abscess was aspirated but still he did not show signs of improvement in his general condition. He was, therefore, sent by me on 28th May, 1943, for x-ray pictures of his lumbar spine and both lungs (see figures 1 and 2, plate XXIX).

To my great surprise the radiologist's report read as under :—

1. No radiological evidence of disease of lumbar spine.

2. Radiological evidence of multiple stones in the right kidney and a big stone in the left. Size of kidneys not properly visualized, but the lower poles are at lower level than normally seen.

3. Of lungs—Hilar shadow with calcified glands. Infiltration right lung particularly middle zone. Right apex also looks infiltrated. Left is free. Costophrenic angles are free. Cupolas regular. Heart shadow is normal.

After x-ray examination his urine was examined and the result is noted below :—

Urine.—Pale yellow colour, strongly acid, specific gravity—1024, deposits of yellow colour ++ present, albumin +, pus +, no sugar or acetone.

Microscopically there are large deposits of pus.

The case appears worthy of record as during my experience a case with such large and multiple stones without any renal symptoms has never occurred and is hard to believe. For his lung condition he has been sent to a sanatorium.

Recently two small stones were discharged through a small opening in the skin near the lower pole of the right kidney.

My thanks are due to Dr. C. D. Newman, Chief Medical and Health Officer, N. W. Railway, for permitting this article to be published.

A STUDY OF 'CHOLERIFORM' DISEASE IN THE TYPHOON AREA OF CONTAI

By A. P. JANA, M.B.

Contai

It was on the 16th of October 1942 that the great cyclone passed over Contai. One result

of the cyclone was that all the tanks, wells, pools and puddles were polluted and contaminated by the decomposition of leaves, plants, trees, corpses and carcasses and other organic matter. Probably a fortnight after this day of deluge, sporadic cases of cholera began to be reported daily from the different parts of the sub-division. Apprehending an outbreak of the disease in epidemic form in the near future, the Government and benevolent institutions took certain measures, opened centres of medical relief and started inoculation of all the people of every village throughout the affected area. Soon the epidemic broke out with all its virulence. To cope with this situation, the services of medical practitioners of every description were solicited. Unable to remain an indifferent spectator, I took charge of one of the centres and had ample opportunity to study many cases of the 'choleric form' condition.

Signs and symptoms.—The signs and symptoms in these cases resembled in many respects those of cholera. They started with watery motions, at first faeculent or offensive, but soon after the odour gradually turned 'fishy' and the colour changed, and the motions became greenish or slightly reddish, or colourless like water. In very few cases I saw the 'rice water' stool. In these watery stools, in almost all cases, there was a sediment of flakes of intestinal mucosa. There was no tenesmus but in some cases there was griping, and in a very few cases (which were more fulminating) there was neither tenesmus nor griping. There was often intense thirst, but milder cases had no thirst.

After three or four motions, vomiting started and evacuation went on by both routes, and there was suppression of urine. The temperature was subnormal from the very beginning. In some cases collapse set in very early. Spasm of muscles commenced after a few evacuations. All the toxæmic symptoms became more or less manifest in all cases. There were uræmia and anuria with all their symptoms just as in cholera cases. In a word, all the signs and symptoms of typical cholera were present with the special characteristics of stool mentioned above.

Diagnosis.—The only disease with which these so-called cholera cases could possibly be confused is bacillary dysentery. The points in favour of my diagnosis of bacillary dysentery are:—

(a) Stools of these acute cases were not like the typical 'rice water' stool of cholera: the watery stool had rather a greenish or a reddish tinge with sediment of shreds of intestinal mucosa.

(b) After injection of anti-dysentery serum the colour of the stool became more or less greenish, gradually less in quantity and frequency.

(c) The cure-rate amongst those cases which received anti-dysentery serum was 60.7 per cent against the cure-rate of 26.6 per cent of those

who did not receive the serum: other treatments being the same in both groups.

(d) The occurrence of the condition in a fair number (52 per cent of the patients) of those who had received anti-cholera inoculation recently and were thus not likely to get cholera.

(e) The absence of tenesmus in any of my cases and the absence of griping in more than 50 per cent of cases were possibly due to the fact that the toxin of dysentery bacilli might have paralyzed the splanchnic nerve endings.

(f) All the houses in the area where the epidemic broke out were full of bacillary dysentery cases of varying types and duration.

Comments.—Manson noted that such choleric form types of bacillary dysentery having all the symptoms of cholera and subnormal temperature from the beginning were by no means frequent. This year we find that this type of disease is predominant throughout the sub-division, particularly in the saline-water inundated area, where cases are of more fulminating type. The rise of temperature due to some specific infection is the result of response of the defensive system of the body, but in these cyclone-affected and inundated areas, people were so much devitalized that their defensive system failed to respond to the infection, and thus there was no rise of temperature. The subnormal temperature was also due to drainage of large quantities of serum from the body. Lack of mucus in the stool was due to the lack of inflammatory reaction of the intestinal mucosa, which was again a result of the lack of response of the defensive mechanism of the body to combat the infection. If in these cases a certain degree of immunity was supplied by giving anti-dysentery serum, or if the patient survived for a certain period, the temperature might rise and in fact in some cases after the stoppage of motions there was a certain degree of fever and the mucus appeared in the stool.

Previously I never found such types of bacillary dysentery in my practice of about 15 years, and such is the experience of most of my fellow practitioners here. It may be that the abnormal situation and the abnormal loss of vitality caused in general by the cyclone have created a good field for this epidemic of atypical bacillary dysentery.

My hearty thanks are due to Dr. A. C. Datta, Public Health Officer, Contai, for his kind suggestions and valuable assistance without which it would not have been possible to publish this note.

ERRATA

In the article 'Intestinal Tuberculosis: Its Diagnosis and Significance in the Treatment of Pulmonary Tuberculosis' by J. Frimodt-Møller, in the October issue of the *Gazette*—

On p. 508, table II, under the percentage column, the figures 84.9 should read 41.0, and 41.0 should read 84.9.

On p. 514, first column, 18th line from the top, '67 cases' should read '60 cases'.

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Indian Medical Gazette

DECEMBER

MARKED EOSINOPHILIA WITH LUNG INFILTRATION

THE eosinophils of the blood are few in number, constituting normally 2 to 4 per cent of the total white cell count. The normal average figure is not infrequently higher among the Indians, especially among the Assam population, where the hookworm infection rate is nearly 100 per cent. The function of the eosinophils is not clearly known; they do not appear to be phagocytic. In certain infections, while the neutrophils increase, the eosinophils tend to decrease or disappear, but reappear with the onset of convalescence, and may even increase considerably after the infection is overcome, as in scarlet fever. Their number in the blood is often increased in asthma, hay fever, and other allergic states. Eosinophilia is frequently a characteristic of helminthic infections, *viz.*, ancylostomiasis, filariasis, trichiniasis and hydatid disease. It is sometimes a feature of certain skin diseases, notably dermatitis herpetiformis, urticaria and pruritus. Occasionally, it occurs in lymphadenoma. In these conditions the proportion is usually within 20 per cent. Very marked increase may occur in trichiniasis and 'eosinophilic leukaemia'. Then there is the Löfller's syndrome, with moderate leucocytosis and eosinophilia with temporary localized pulmonary infiltrations, possibly due to the migration of helminthic larvae in the lungs. The so-called hereditary eosinophilia is a rare condition which manifests itself in different members of a family. Finally, there is 'idiopathic' eosinophilia which is not uncommon in India; in some cases it has been attributed to syphilis, or to the after effect of helminthiasis or skin diseases which are so prevalent here.

Recently, several writers in India have described a syndrome or disease entity characterized by eosinophilia, pulmonary infiltrations, attacks of bronchial asthma and other general symptoms. Three years ago, in a study of 600 patients with 20 per cent of eosinophilia or more, Frimodt-Møller and Barton found 175 of them showing in x-ray picture an evenly distributed extensive mottling of small nodular shadows over both lung fields, with increased linear markings somewhat resembling miliary tuberculosis or silicosis. The highest eosinophil count was 85,000 per c.mm. and the highest eosinophil percentage was 92. The prominent symptoms were cough, fever and loss of appetite, but in 20 per cent of the patients there was asthma or bronchitis. Some of them were seen again several years later when they showed the same condition, especially in the x-ray and blood picture.

These patients were seen in a tuberculosis sanatorium where they had been sent because of the suspicion of tuberculosis.

Early this year Weingarten gave a fuller clinical account out of a series of 81 cases. According to him the symptoms begin with lassitude, fever rising to 100° or 101°F. and loss of weight followed by a dry hacking cough, expiratory dyspnoea and in some cases severe attacks of typical bronchial asthma, the patient remaining comparatively free from these symptoms in the daytime. After some weeks the temperature becomes normal, but the paroxysms of coughing and in many cases the 'asthmatic' attacks persist at night, and the condition tends to be chronic. Physical signs somewhat resemble those of bronchitis or asthma. The spleen is enlarged during the febrile period. If there is any expectoration, the sputum is scanty and tenacious and contains clumps of eosinophils but no Charcot-Leyden crystals or Curschmann's spirals. The most striking feature is massive eosinophilia causing considerable leucocytosis, the percentage of eosinophils, which are usually of normal size and shape, reaching as much as 88 per cent. The x-ray picture of the chest shows disseminate mottling of both lungs.

Subsequently, a number of more or less similar cases have been reported by other observers and more are now being seen, all in India, attracting considerable attention. We are including in the present number three papers dealing with this subject based on case reports.

Although often a chronic disease, it runs a benign course, and so far no fatal case has been reported. Even without treatment the condition gradually appears to improve spontaneously, the blood findings, however, according to Simeons, never becoming normal; and for no apparent reason, exacerbations occur sometimes at intervals of years.

During the short period of its recognition, the condition has already acquired several names, such as 'pseudo-tuberculosis of the lungs with eosinophilia', 'eosinophil lung', 'tropical eosinophilia' and 'benign eosinophil leukaemia'. The aetiology remains obscure. All classes of society and all races are affected. Most of the cases have been reported from South India. The usual causes of eosinophilia could be excluded, although in Frimodt-Møller and Barton's series 48.2 per cent had infection with hookworm and other intestinal parasites, but the infection rate was even less in those with the highest eosinophil count. Many of Weingarten's patients were living near the sea and he thought that it was common there. Many of the cases had been diagnosed and treated as pulmonary tuberculosis or chronic bronchial asthma, but the sputum contained no tubercle bacilli, and the x-ray findings were not quite typical of miliary tuberculosis with which it could be mistaken. As regards asthma, typical attacks were not seen in many cases, but it seems that a considerable

proportion of the patients was suffering from mild attacks of asthma. In any case, the paroxysms of coughing, eosinophilia, pulmonary infiltrations, eosinophils in the sputum and periodic recurrences appear to be the result of an allergic response to some antigen. There is evidence to show that in allergic states there is active involvement of the blood vessels in the lungs, skin or other tissues, characterized by increased permeability of their walls and perivascular infiltrations of eosinophil cells giving rise to protean manifestations. The lesions in the lungs in this condition are apparently due to these infiltrations. One striking feature is the very high eosinophilia which is often out of all proportion to the general symptoms. The condition however deserves further investigation, and more evidence is needed on the ætiology and nature of the condition.

Treatment was at first purely symptomatic. One of Weingarten's patients contracted syphilis for which he was treated with neoarsphenamine. After four injections when the white cells were counted, it had fallen from 64,200 to 7,800 per c.mm., and the eosinophils had decreased from 71 to 16 per cent. His subjective symptoms had also vanished. Weingarten has reported uniformly good results with the drug and this is borne out by the reports from other writers. After the first two or three injections there may be a further slight increase in the total leucocyte count as well as in the percentage of eosinophils; later with a few more injections they suddenly diminish. Other arsenicals such as acetylarsan and mapharside are equally good in the treatment. Simons says that since adopting this line of treatment, he has never seen a relapse, and incidentally he mentions that he had noted great improvement with liver injections but the abnormality in the blood increased. This was to be expected as the eosinophils generally tend to increase after liver administration.

It is worth remembering this condition in every case of chronic febrile cough in which there is no evidence of tuberculosis.

R. N. C.

THE ALDEHYDE TEST

In a recent number of the *British Medical Journal* appears a note from Colonel Spackman, I.M.S., Inspector-General of Civil Hospitals, Bihar, in which he points out that the aldehyde test for kala-azar was not originated by the worker whose name is commonly attached to the test (i.e. Napier).

Colonel Spackman states that the peculiar reaction of the serum of cases of kala-azar in this test was discovered by him in 1921 and that he communicated his findings to the *British Medical Journal* (in which a note was published in August 1921) and to the School of Tropical Medicine which confirmed findings and developed the use of this test in kala-azar.

Colonel Spackman in a letter to the editor has stated that Mackie and co-workers in Assam independently made the same discovery in 1921. The test in kala-azar apparently owes its origin to Spackman and to Mackie, but Napier at the School of Tropical Medicine, Calcutta, confirmed it, described the technique in detail, established its value and limitations, and popularized it.

The name sometimes used for it, the Napier test, is therefore a little misleading. Napier himself usually referred to it as the aldehyde test, and this name is generally used in the School of Tropical Medicine.

'ANDROPHILIC' MOSQUITOES

SIR HAROLD SCOTT in a recent review* of Sir Philip Manson-Bahr's *Synopsis of Tropical Medicine* draws attention to the fact that the word 'androphilic', which Manson-Bahr uses and which is commonly used by other writers to indicate the habits of mosquitoes of feeding on man, is incorrect. As Scott points out, an 'androphilic' mosquito is equally 'gynæcophilic'. Scott suggests the word 'anthropophilic' which covers both.

* *Trop. Dis. Bull.*, May 1943, p. 15.

Special Article

PROCESSING OF LIQUID SERUM

By D. L. SHRIVASTAVA

(From the Indian Red Cross Blood Bank, Calcutta)

THE technique of processing the liquid serum described below was in use in the Calcutta Blood Bank till the arrival of the pilot Seitz filter a few months ago. A start was made with the technique published by Hayes *et al.* (1942) which the author of this paper had the opportunity to work with during the latter part of 1941 at Lahore. A large number of additions and alterations had to be made from time to time to suit the requirements of this Bank, and so it was considered of interest to publish the details. The aim has been throughout to make the apparatus more suitable for working with large amounts of serum in a closed system.

Laboratory.—One has to be very careful about the sterility of the laboratory, specially when large batches of serum have to be processed. The whole of the filtration laboratory in Calcutta is air-conditioned, and the air injected into the room is filtered through a 'visco filter' and a 'replacement filter'.

The laboratory is divided into three sections. First is the ante-chamber in which the apparatus is fitted up for sending out for sterilization, and in which the workers dress up. Through this section one enters the second section where pooling and filtration are carried on. The serum

filtered here is led through a rubber tube into the third section, the bottling cabin, where the serum is filled into transfusion bottles by the technique described below. The upper segments of the walls of the bottling cabin are made of metal gauze so that conditioned air can circulate inside it. This cabin is steamed on the eve of the filtration day and the whole laboratory is sprayed every morning and evening with 2 per cent dettol or chlorosol by means of a spray gun at a pressure of 10 to 12 pounds. Spindle oil is spread once a week on the floor which is covered with linoleum. In one of our latest tests of the sterility of the room by means of Well's centrifuge 8 organisms were found per cubic foot of air. This is expected to be brought still lower. Agar plates are exposed every now and then to keep a check on the sterility of the room.

The top of the working table is covered with maekintosh which is scrubbed with a solution of lysol and before putting any piece of sterile apparatus on it, it is covered with sterile towels. The workers put on sterile aprons, masks, gowns, gloves and shoe covers and while working observe all the precautions of the operation theatre. Greatest care is taken to see that no worker touches any part of the apparatus that may come in direct contact with serum.

Cleansing of the apparatus.—The importance of a thorough cleansing of the component parts of the apparatus with which serum comes in contact cannot be over-emphasized. Proper attention to this will obviate many unpleasant reactions usually attributed to pyrogens. New rubber tubes and bungs are first boiled in 5 per cent caustic soda solution for 20 minutes and then thoroughly washed till the washings are neutral. After every two or three experiments, the parts are boiled in 2 per cent sodium carbonate solution. The glass parts are properly washed and then dipped in acid cleaning fluid (potassium dichromate and sulphuric acid) overnight, followed by washing with water to get rid of all the acid. Just before setting up the apparatus for sending out for sterilization, every piece is washed individually inside and out with fresh distilled water and boiled in fresh or sterile distilled water for 20 minutes. The apparatus is then fitted and packed up in trunks for sterilization which is done within two to four hours of fitting. After use, the apparatus is immediately dismantled and soaked in water. Glass parts are disconnected from the rubber ones, and tap water is forced through every piece. A cotton tape is passed through each tube to dislodge clots of blood or particles of serum that may be sticking to the inner walls of the tube. After this, tap water is again forced through the tube, followed with distilled water.

Sterilization.—Apparatus is sterilized inside trunks at 20 pounds pressure for 30 minutes and anything used for filtration is sterilized twice. Gloves are properly cleaned with soap, dried and dusted with french chalk and packed

individually inside coarse cloth bags, which are put inside a drum and sterilized at 5 pounds pressure for 25 minutes. Aprons, masks and head covers are sterilized at 15 pounds for 30 minutes.

Pooling.—The clotted blood is allowed to stand in the cold room at 4° to 5°C. for 72 hours, after which it is taken into the laboratory for pooling. Samples showing excessive amounts of hæmolysis or lipoids are discarded, and the rest are pooled. It has been found that if 18 to 20 samples of serum are pooled, the agglutinin titres of the final serum are usually below $\frac{1}{8}$. In actual practice 70 to 80 samples are pooled in 10-litre bottles. Since the serum is finally to be filtered, a positive Wassermann or Kahn is not considered a disqualification for the particular sample being pooled with others (Whitby, 1942).

The serum is aspirated out of the bottles in a closed system as shown in figure 1, which is self-explanatory. The 10-litre bottles (A) are fitted up with rubber bungs with necessary glass and rubber tube connections and packed inside trunks. A fresh pooling needle (8½ inches long and 1 mm. internal bore) is used for each bottle of blood. These are also autoclaved in packets of 12 inside the trunks. Any open end of the rubber or glass tubing is covered up with one layer of unglazed brown paper and tied. After autoclaving, the parts are taken out of the trunks under aseptic conditions and arranged on the working table the top of which is covered with sterile towels. Connections are made after proper flaming with a burner autoclaved with the rest of the equipment. For aspirating out the serum, a vacuum of about 15 inches produced by a filter pump is used, and great care is taken to see that as little clot as possible is sucked over with the serum. This is done by carefully regulating the speed of aspiration with the help of glass stop-cock (G) in the circuit.

After the pooling is finished, the vacuum in the system is broken through the air filters by closing the screw pinch-cock (5) and opening the cocks numbers 1, 2, G, 3 and 4. The rubber bungs are then taken out of the bottles under the flame, and sterile ones without any holes are inserted instead and wrapped up with cellophane up to the neck of the bottles and tied. The pooled serum is allowed to stand in the cold room (4° to 5°C.) for 18 to 48 hours. During this period, the agglutinins get absorbed by the respective agglutinogens.

The apparatus shown in the figure 1 is for two workers, but it can be easily adapted for more. The two workers who are pooling the serum are aseptically dressed. Besides these there are two others, who are also aseptically dressed but do not have gloves on. One of them removes the bottles already pooled and supplies a fresh one after flaming the top of the aluminium cap, and the other worker removes the used needles for cleaning. With this set of 4 workers it is possible to pool 70 to 80 bottles in one hour.

Transfusion bottles.—The bottles are properly cleaned with acid, washed and dried. Rubber washers ($\frac{3}{16}$ -inch thick) are first washed and boiled in 5 per cent solution of sodium hydroxide for 20 minutes to get rid of the excess of sulphur. They are then washed with tap water followed with distilled water till they are free from alkali. The bottles are plugged with cotton and the top is wrapped up in a single layer of brown paper. The aluminium caps with rubber washers properly fitted in them are also wrapped in a single layer of paper and tied to the neck of the respective bottles, which are then autoclaved at 20 pounds pressure for 30 minutes. After this, they are packed inside trunks having partitions made in them, and are autoclaved once again along with the rest of the apparatus for filtration.

Fitting of the apparatus.—After autoclaving, trunks are cleaned and taken inside the laboratory, where the contents are taken out by an aseptically dressed worker and put on the table already covered with sterile towels. The apparatus is fitted up as shown in figure 2. Open ends of tubes are carefully unwrapped and after flaming are connected up. The Seitz filters are all tightened and connected as shown in the figure, with the necessary precautions of flaming, etc. The rubber tube carrying the filtered serum is led through an opening into the bottling cabin and connected to the filling hood (H). The hood rests on a small table covered with sterile towels. On an adjacent table, covered with sterile sheet of cloth, are placed the bottles taken out of the trunks. These are all covered up with sterile towels till ready for use. After this the cabin is again sprayed with dettol or chlorosol and no one enters the cabin till the serum is ready for being bottled.

The bottle (C) containing the pooled serum is connected, screw pinch-cocks 1, 2, 4, 5 and 6 are opened and 3, 7, 15 and 16 are closed, and the filter pump is started. The serum passes through the clarifier and from there into the serum chamber (E). When the clarification is finished, stop-cocks 1, 4, 5, 6, 9, 10, 11 and 12 are closed, and 3, 7, 8, 13 and 14 are opened, so that the serum from the chamber (E) flows into the Seitz filters. When the pads get soaked, the nuts of the filters are further tightened, to avoid leakage. It is always advisable to let the serum flow into the filters without the application of any positive pressure higher than the one exerted by the column of the serum in the chambers, so that the pads may get soaked slowly, without any danger of their being damaged by a sudden rush of serum at a high pressure. When the serum starts coming out of the Seitz filters, the open end of bottle A is connected to the positive pressure line, and a pressure of about 2 pounds is applied in E. This pressure is gradually increased to 4 to 5 pounds during the course of filtration.

Just as soon as the bottle G is filled with the filtered serum, pinch-cock 9 is opened and 8 and 13 are closed to let the serum flow into

G₁ and to stop its flow into G. The pinch-cocks 10 and 12 are then opened for emptying G₁ into the transfusion bottle lying under the hood (H). For this the cotton plug of the transfusion bottle is removed under a flame, the neck and the mouth flamed and the bottle is placed under the hood. The pinch-cock 15 is cautiously opened to apply a slight positive pressure inside G and thus let the serum flow into the transfusion bottle. When the serum reaches the 500 c.cm. mark on the transfusion bottle, the cock 12 is closed, the bottle is removed from under the hood and another is put instead for filling. The filled bottle is flamed and the aluminium cap, after careful unwrapping, is put on the bottle and tightened, care being taken all the time that the whole operation is done as near the flame as possible and, while putting the cap, the open end is kept down and the rubber washer is not touched with the finger. After tightening the cap, the bottle is gently inverted to test for any leakage. When G is completely emptied, cocks 10, 12 and 15 are closed and 13 opened to release the pressure in G. The transfusion bottles and also the sterility test samples are taken out of the cabin as described later for sealing. The two holes on the top of the metal cap and the junction of the metal and glass are properly sealed with a mixture of equal parts by weight of bees-wax and rosin boiled to a temperature of about 160°C. As a further precaution against leakage from the aluminium caps, a viscap is put on the top of the metal cap. After this the bottles are labelled as follows:—

SERUM

Red Cross Blood Bank Committee, Calcutta

Batch No.....Bottle No.....

Filtered on.....

Important

Store in a refrigerator or a cool dark place. Maximum temperature must not exceed 105°F. On storage fat and soaps may appear as a grey layer on top of the serum. Such serum may be used. If shaken in transit, fat will make the bottle contents cloudy. Allow to settle. If serum remains uniformly turbid after several days, do not use. In all cases of doubt return to issuing unit, never throw away.

The sterility test samples are numbered separately.

The above process is repeated with serum filled in G, and G alternately till the whole of the clarified serum has been finished.

For filtration one requires 4 workers dressed aseptically and a fifth one, who puts on sterile gown, mask, head and shoe covers. Of these, two aseptically dressed ones remain inside the bottling cabin and two outside. Inside, one is

responsible for filling the bottles and the second one for removing the bottles from under the hood and capping them. Outside, one manipulates the filtration apparatus and the other one does the sealing and viscapping of the filled bottles. The fifth worker labels the bottles and renders any help that the clean workers may need.

The pressure used during filtration is from 3 to 5 pounds and the average speed of filtration is about 2 litres per hour per pad. If the serum is properly clarified, 3 litres can be easily filtered through one pad. Even 4.5 litres of serum have been filtered per pad without in any way affecting the quality of the filtered serum. With the above team, it has been possible to filter about 50 litres in one day by using 11 or 12 filters.

Filtration with a pilot Seitz filter.—A pilot Seitz filter is capable of taking 19 pads of 8 inches by 8 inches size, and it is possible to clarify as well as sterilize the serum within the frame work of the filter by means of a bye-pass arrangement. Therefore the clarifying chamber shown in figure 2 is not needed. Besides this, a large number of connections are avoided, which is a very great advantage from the point of view of the sterility of the final product. The pooled serum is pumped into the serum chambers and from there into the filter. The filtered serum is led into G or G₁ as shown in the post Seitz connections of figure 2. In between the outlet of the filter and the Y-tube leading to G and G₁ is interposed a T-tube to take out the saline solution (about 30 litres) that is first passed through the filter to wash away any loose fibres from the filter pads.

Sterilization of the filter is done by fitting the required number of pads loose and packing the whole thing inside a trunk, as is done with the filtration apparatus described above. The clarity of the serum improves considerably if single clarification pads and double sterilizing pads are used. This cuts down the speed of filtration but it is worth while. With a maximum pressure of 6 to 7 pounds it is possible to filter about 80 litres in 4 hours of actual filtration.

Sterility test samples.—Samples of about 15 c.cm. for sterility tests are taken out in transfusion bottles sterilized along with others inside the trunk. These are stoppered, sealed and viscapped like the other bottles. In any particular batch one such sample is taken for every 12 litres, with a minimum of 3 and a maximum of 5 samples taken at regular intervals. With each sample taken as above, another 5 c.cm. of serum is run into 50 c.cm. of glucose broth in a transfusion bottle, which is capped, sealed and viscapped like others. The sterility tests are done by the Microbiology Department of the Institute by running 5 c.cm. of serum from each sample into 50 c.cm. glucose broth tubes. One such tube is incubated aerobically and the other anaerobically. The

results are declared after 72 hours' incubation, and in case of doubt the incubated broth is plated out. The glucose broth bottles are incubated for 5 days, and then examined. The results obtained serve as a sort of supporting evidence for those obtained by the regular sterility tests. In case of any discrepancy between the two results, the latter gets the preference. If more than 50 per cent of the sterility samples taken show contamination, and if the bottles of serum are still quite transparent, they are immediately refiltered. Such an occasion, however, is indeed very rare, if proper care is taken in carrying out the technique of filtration described above. Only once during the last twelve months a small batch had to be refiltered.

Storage at 80°F.—All the bottles of filtered serum are stored in the laboratory at 80°F. for at least 3 weeks, after which each bottle is examined individually against a light. Any bottle that is not quite transparent is discarded, and if the percentage of such discards goes above 5, the batch in question is rejected. Actually the number has so far never gone above 1 to 2 per cent. Once in a while a bottle may be found contaminated due to a small crack in the bottle which escaped detection during filling. Such bottles are naturally not counted in the discards mentioned above.

Storage at 40°F.—After storage at 80°F., the bottles are transferred to the cold room at about 40°F. (4°C.), where they stand till required. During the storage in cold, lipoids and calcium soap particles appear in the serum. These float on the top, leaving the bulk of serum quite transparent, and can be easily filtered off in the giving set by inserting a piece of gauze in one of the glass tube windows.

Issue of the serum.—A regular account is maintained of the number of bottles prepared, stored and issued. While issuing, each bottle is individually examined against a light inside the cold room and any suspicious looking bottle is held back for testing. The following instructions are issued with the serum:—

Instructions for the use of serum

1. Cut open the viscap or untie the cellophane covering on the top and the waxed cotton tape.

2. Loosen the metal cap.

3. Hold the serum bottle in a slightly slanting position, remove the metal cap, and insert the rubber cork containing the long air inlet and the short serum outlet tubes tightly into the neck of the bottle, and fasten by means of adhesive tape.

- 3a. Tighten the screw clip on the air inlet tube.

4. Invert the bottle gently and hang it at a suitable height. The speed of flow of serum can be adjusted by means of the clip put on either the serum tube or the air inlet tube. It is better to transfer the screw clip on to the serum tube.

5. Get rid of the air bubbles in the tube before putting the serum into the vein of the patient by allowing about an ounce to run out freely.

5a. If more than one pint is needed for transfusion, stop the flow while the layer of serum in the first bottle is still above the tip of the short glass tube. Now tighten the screw clip on the air inlet tube. Take out the rubber cork with glass tubes gently and fit into the next bottle of serum, following the same precautions as before.

6. If there be lipoids and calcium soap particles floating on the top of the serum, it is best to insert a piece of clean and washed gauze *lightly* in the window nearer the drip bulb, before fitting up the transfusion set for auto-claving. This may, however, be unnecessary if the bottle be inverted gently while starting transfusion. Particles will float up to the top.

7. After use, the transfusion set should immediately be soaked in water and subsequently cleaned with running tap water followed by distilled water.

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Medical News

ROYAL COLLEGE OF SURGEONS OF ENGLAND

REGULATIONS FOR THE F.R.C.S.

THE Council of the Royal College of Surgeons of England has revised the regulations for the Fellowship, and the *primary* examination beginning on 29th November next will be the last to be conducted under the present regulations.

New regulations have been approved by the Council and will become effective as from the end of 1943.

These regulations embody the following changes:—

(i) The *primary* examination cannot be taken by undergraduates, but will be open only to members of the College, or to graduates in medicine and surgery of the universities and medical colleges recognized by the Council for the purpose, who are able to comply with the conditions of the regulations.

(ii) The subjects of the *primary* examination will be:—(a) *Anatomy (including Normal Histology)*, and (b) *Applied Physiology and the Principles of Pathology*. A synopsis indicating the general scope and spirit of the examination in *applied physiology and the principles of pathology* is published in the new regulations.

With regard to the *final* examination, no candidate will be admissible without producing evidence of having been engaged in the acquirement of professional knowledge for not less than two years subsequent to the date of having obtained the membership of the College or some other recognized qualification, *vide* (i) above.

The dates of the examinations have been re-arranged, so that it will be possible for candidates who pass the *primary* examination to proceed immediately to the *final* examination, if they are eligible. During 1944 the examinations will begin on the following dates:—

Primary examination—24th April and 23rd October.
Final examination—4th May and 2nd November.

Copies of the new regulations and full particulars may be obtained, post free, from the Director of Examinations, Examination Hall, Queen Square, London, W.C.1.

KENNEDY CASSELS.

Secretary,

Royal College of Surgeons of England.

June 1943.

INDIAN MEDICAL COUNCIL

IN exercise of the power conferred by clause (d) of sub-section (1) of section 3 of the Indian Medical Council Act, 1933 (XXVII of 1933), the Central Government is pleased to nominate Colonel J. B. Hance, C.I.E., O.B.E., V.H.S., I.M.S., Director-General, Indian Medical Service, to be a member of the Medical Council of India, with effect from the 4th October, 1943, *vice* Lieutenant-General Sir Gordon Jolly, K.C.I.E., K.H.P., I.M.S., resigned.

Current Topics

The Bactericidal Effect of Tin and Its Application to the Treatment of Typhoid Fever

By RUDOLPH REITLER, M.D.

and

KURT MARBERG, M.D.

(Abstracted from the *Transactions of the Royal Society of Tropical Medicine and Hygiene*, Vol. XXXVI, March 1943, p. 305)

1. METALLIC tin has a slow bactericidal effect on certain micro-organisms, amongst them *E. typhosa*.

2. A drug containing tin stearate and colloidal metallic tin had a favourable effect in typhoid fever, decreasing the death rate to 3 per cent in 100 selected severe cases, while the average death rate of a control group of 428 patients including the mild cases was 8.2 per cent. It is very probable that the duration of the disease is shortened and that in a certain number of cases the toxæmic condition is improved. We are inclined to attribute these effects to the rather unique coincidence that drug and causative organism have a common place of accumulation, namely the intestinal lymphatic nodes. But it may still be open to discussion whether the action of the metal there is as simple as we supposed it to be, or whether it is rather of an indirect nature, consisting in a stimulation of cellular antibacterial activity.

3. The earlier treatment is started the better seem to be the prospects of success.

4. Two healthy typhoid carriers were treated with the same drug and lost their bacilli after taking it, with intermissions, for three weeks and five months respectively.

The Preservation of Vi Antigen in T.A.B.C. Vaccine: With a Note on Combined Active Immunization with T.A.B.C. Vaccine in Tetanus Formol-Toxoid

By S. G. RAINSFORD

(Abstracted in the *British Medical Bulletin*, Vol. 1, March 1943, p. 10, from *Journal of Hygiene*, Vol. XLII, May 1942, p. 297)

It is essential that T.A.B.C. vaccines for use in the Navy should, in addition to possessing unaltered O and Vi antigens, be able to retain these antigens in active

form when stored for many months at 23°C. to 25°C. The antigens are fully retained in vaccines sterilized by merthiolate, colloidal silver, alcohol or acetone, but, while these agents may be successfully used as preservatives when the vaccine is stored in the ice-box, the Vi antigen, as detected by its power to stimulate Vi antibodies in the rabbit, is seriously impaired in a few months at 23°C. to 25°C.

The author's experiments were directed to finding a means of increasing the heat stability of the Vi antigen and in this he was assisted by the observation that exposure to short periods at 37°C. or 60°C. has the same effect as exposure to long periods at 23°C. The key to the problem appeared to be dehydration of the bacilli, and vaccines desiccated by acetone or suspended in 32 per cent saline were found to retain Vi antigen for a year at 23°C. to 25°C. The protocols show that a vaccine sterilized by 1/2,000 merthiolate in 32 per cent saline and preserved with 1/10,000 merthiolate in 32 per cent saline still stimulated in rabbits a high titre of O and Vi antibodies after 21 to 50 days at 37°C. and after at least 6 to 7 months (the longest time yet available) at 23°C. to 25°C., and that the antibodies were fully potent in the mouse-protection test.

In view of recent work (Felix, 1941; Felix, Rainsford and Stokes, 1941) on T.A.B. vaccines sterilized and preserved with alcohol, it may be noted that the present author reports that a vaccine killed by 75 per cent alcohol in physiological saline, washed and resuspended in 25 per cent alcohol in saline retained little or no Vi-stimulating capacity after 21 to 30 days at 37°C. No information is available regarding the behaviour of this vaccine at lower temperatures.

Full details are given of the preparation of (1) dried T.A.B.C. vaccine to which the necessary volume of merthiolate in saline, issued separately in a vaccine bottle, is added by syringe just before use, and (2) T.A.B.C. vaccine using 32 per cent saline with merthiolate. The latter is easier and cheaper to prepare and is to be preferred for routine work.

The effect of mixing T.A.B. vaccine with tetanus formol-toxoid was also examined. The results suggest that this procedure, owing to the formol or to the phenol used to preserve the toxoid, results in a marked decrease in the immunogenic properties of the Vi antigen. The phenol cannot be replaced by merthiolate as the bacteriostatic properties of the latter are destroyed by sulphur derivatives (sodium metabisulphite is used to neutralize the free formalin after toxoiding). The addition of tetanus formol-toxoid to dried vaccine just before administration did not solve the problem, which must await further enquiry.

The author points out that the older vaccines, though inferior to the newer types in experimental immunization against typhoid, are nevertheless known to have been valuable in practice, perhaps owing to their ability to sensitize the tissues to Vi antigen, and that it is not known how admixture with formol-toxoid affects this property.

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Lytic Agent and Inhibitory Factors in Human Tissue and Sera

By B. G. MAEGRAITH, M.B., D.Phil., B.Sc.
 G. M. FINDLAY, C.B.E., M.D., D.Sc., M.R.C.P.

and

N. H. MARTIN, D.M., M.R.C.P., F.I.C.

(Abstracted from the *Lancet*, Vol. I, 8th May, 1943, p. 573)

1. HUMAN tissues have been shown to lyse saline suspensions of washed red cells.
2. Human sera have been found to inhibit this lysis.

3. The activity of the inhibitory factor in sera from cases of blackwater has been titred out and found to be reduced during hæmolytic crises.

4. An explanation of the increased hæmolysis in blackwater fever is, that the reduction in the activity of, factor has disturbed the balance of lytic agent and inhibitor to the lytic side.

Immune Serum for Mice infected with *Leptospira icterohaemorrhagiae*

By C. L. LARSON

(Abstracted from the *Public Health Reports*, January 1943)

CONSIDERABLE debate has arisen over the value of convalescent or hyperimmune serum in the treatment of spirochætal jaundice (Weils' disease), but little experimental work has been done to clarify the subject. These experiments on mice were designed to test this question and to indicate the value of specific immune serum as a therapeutic agent among mice suffering from leptospirosis. Convalescent serum from human beings and hyperimmune serum and plasma and normal serum from rabbits were employed. The method of testing the therapeutic efficacy of these substances included titration of the infective agent, titration of specific protective antibodies in the specimen of serum or plasma to be tested and inoculation of this material into infected mice at suitable intervals in order to observe the therapeutic effects. It was found that serum from patients convalescent from spirochætal jaundice and immune rabbit serum and plasma all prevented the death of young white mice infected with *Leptospira icterohaemorrhagiae*. The effect of these materials was enhanced if administered on or before the fourth day after infection.

Prostatic Cancer and Castration

(From the *Lancet*, Vol. I, 6th February, 1943, p. 177)

AMONG the many difficulties in treating cancer of the prostate are its insidious onset, the anatomical obstacles to radical extirpation, and its high resistance to x-rays. Lately Huggins in Chicago has advocated castration in these cases, especially when metastases are present in the bones. The operation is not claimed as a cure, but is said to relieve pain and perhaps to retard tumour growth. The claim is rational and based on physiological knowledge, apart from case histories, and is supported by other surgeons, including Lane in this issue.

About 150 years ago John Hunter pointed out that the prostate owes its activity and perhaps its existence to the testicles, removal of which causes atrophy of the gland. Furthermore, it is recognized that cancer cells may be sufficiently differentiated to produce hormones like those naturally formed in health or to respond to hormonal stimulation in the same way as normal cells; the prostate exemplifies both these propositions. In response to testicular hormones the healthy adult prostate forms considerable amounts of acid phosphatase; so also do the osseous metastases of prostatic cancer, and there is apt to be an excess of acid phosphatase in the serum of patients with disseminated cancer originating in the prostate. After castration of these patients the acid phosphatase of the serum often falls. Moreover, there is evidence that the secretory activity of prostatic metastases, like that of the normal prostate, is stimulated by androgen and inhibited by oestrogen. It seems almost certain, if in fact the tumour cells are secretory as they often appear to be, that castration would cause a diminution of their activity and a consequent retarded growth or shrinkage of the tumour; this may explain the relief of pain observed in nearly all of 109 reported cases.

A rational surgical procedure in treating cancer is not always a successful one. At the end of last century Sir George Beatson, rightly assuming that the

cause of mammary cancer lay in the ovaries, advocated oöphorectomy as an ameliorative measure. His suggestion was followed enthusiastically by several surgeons who reported considerable benefits from the operation, but further experience brought disappointment and the operation was soon discarded. Castration for the cure of benign enlargement of the prostate—a simple, rational and successful remedy—died in its infancy, partly because of the rise in favour of suprapubic prostatectomy, but much more because a baseless rumour sped round the world to the effect that castration was apt to cause mental deterioration. The operation as now practised for the relief of prostatic cancer will doubtless dispel this pernicious myth, and that in itself will be an important gain. It may be hoped, also, that this time experience will justify the early optimism. Occasionally sterilization by x-rays has been suggested as though it were an alternative to castration. Such a proposal is fallacious, for though a sterilizing dose of x-rays applied to the testes will arrest spermatogenesis it will not materially affect the production of gonadal hormones by the interstitial cells.

A Rapid Test for the Serodiagnosis of Syphilis

By F. RAPPAPORT
and

F. EICHHORN

(From the *Lancet*, Vol. I, 3rd April, 1943, p. 426)

IDE, Kline, Laughlen and Meinicke have described rapid tests on slides for the serodiagnosis of syphilis but these have several drawbacks. For example, not every positive serum can be detected; slide tests are not suitable for a large series of sera, because of evaporation from the small amount of fluid on the slides; the methods are unsuitable for the examination of cerebrospinal fluid; and recent inactivation of serum is advised and time is therefore lost.

While carrying out examinations of cerebrospinal fluid with scarlet red or Sudan III coloured mastic we found the results satisfactory and constant, and we therefore substituted mastic for benzoin or tolubalsam, for the rapid serological test, by adding the mastic to the Kahn antigen. Sera were inactivated chemically (as in the Meinicke by high salt concentration) and it was therefore important to attain a pH of about 6.2–6.5 (slightly acid to neutral red), since a fluctuation in acidity may either produce a non-specific flocculation of the mastic in negative sera or prevent flocculation in positive ones. The necessary pH can be attained by means of a phosphate buffer solution and the optimum concentration of salts, mastic, antigen and the pH were worked out experimentally.

PREPARATION OF ANTIGEN

Reagent 1 (intensifying reagent), made up of (a) fresh beef heart muscle is chopped up, dried in the incubator or by an electric fan and thoroughly ground to a powder. To 25 g. of dried and powdered muscle in a 250 c.cm. Erlenmeyer add 100 c.cm. pure anæsthetic ether. Shake for 10 minutes and pour off the supernatant ether. Do not discard the ether decanted throughout the whole process of extraction. Repeat extraction three times with 75 c.cm. ether. Dry the powder till free from odour, weigh and return to flask. Add 4 c.cm. absolute alcohol (dehydrated) per 1 g. of powder. Shake for 10 minutes, allow to stand at room temperature for three days, shake again for 10 minutes and filter. To each c.cm. of alcoholic extract add 6 mg. cholesterol.

(b) The ether collected during extraction is evaporated to dryness at room temperature. To 1 g. of residual substance add 10 c.cm. alcohol. Shake for 10 minutes, allow to stand twenty-four hours in the ice-box and filter in the ice-box.

(c) Dissolve 10 g. of mastic in 80 c.cm. of absolute alcohol, in a 100 c.cm. measuring flask, by heating in

a water-bath. After standing two days in the ice-box add alcohol to make the volume up to 100 c.cm. and filter. Saturate (a) and (c) with a red fat-soluble dye (scarlet red) and filter or centrifuge. To 10 c.cm. of (a) add 1 c.cm. of (c) and 0.2 c.cm. of (b) to make reagent 1. Reagent 1 is stable for about two months; (a), (b) and (c) are separately stable for a very long time; (a) and (b) are kept at room temperature; (c) in the ice-box.

Reagent 2. NaCl .. 9.0 g.
KH₂PO₄ .. 0.63 g.
Na₂HPO₄·2H₂O .. 0.35 g.
Aq. dest. ad 100 c.cm.

Reagent 3 (diluting fluid).
Na₂HPO₄ .. 5.0 g.
Aq. dest. ad 100 c.cm.

Activation of antigen preparatory to use.—To 0.55 c.cm. of reagent 1 add 2.5 c.cm. of reagent 2, the necessary amount of both reagents being previously warmed for 5 minutes in a water-bath at about 30°C. Allow to stand for 5 minutes in the water-bath and add 1.6 c.cm. of distilled water. After 10 minutes the antigen is ready for use and is stable for several weeks if kept on ice.

TECHNIQUE OF TEST

A. *For serum.*—Place one drop (0.05 c.cm.) of serum in a small test-tube (the serum need not be inactivated). Add one drop of antigen. Shake for half a minute and add one drop of diluting fluid. Shake gently for several seconds and examine. In positive cases a strong heavy red precipitate appears; in negative cases the solution remains unchanged. In order to save time when examining many sera it is advisable to read the result after centrifugation for about 2 minutes. In positive cases the precipitation is emphasized.

B. *For CSF.*—In two small test-tubes place 4 and 6 drops of CSF, add one drop of antigen to each, shake for one minute and centrifuge at high speed till the reagent is deposited. Remove the tubes and shake. If, after shaking, the fluid contains distinct red particles the reaction is positive; if the fluid is uniformly clear (as at the beginning of the procedure) the reaction is negative.

In our experience the test described above never failed to show a positive reaction in a positive serum (controlled by other serological tests and clinical evidence); but there were a few non-specific reactions in possibly negative cases, the reason for which we have not yet ascertained. But since we consider this test as a preliminary for excluding negative sera, and since we have controlled positive tests by Kahn, Meinicke or Müller reactions, the few non-specific reactions are not

	Kahn. Meinicke Rapid test		
Number of examinations	5,100	5,100	5,100
Negative cases ..	4,775	4,776	4,765
Positive cases ..	325	324	335*
Non-specific reactions ..	5	4	10†

a serious disadvantage. Further research is necessary to determine the significance of the very few cases where the reaction is considered non-specific. It should be pointed out that non-specific reactions were not found in CSF in a relatively small series of 264 specimens of CSF of which 9 were positive. In our experience of 5,364 sera and CSFs there was no single case where a positive serum or CSF gave a negative reaction.

In several early cases the above rapid test was positive while the Kahn and Meinicke were still negative; a few weeks later the same sera gave a slight positive

* Five of the positive rapid test cases which were at the beginning negative in the Kahn and Meinicke test proved subsequently to be luetic.

† Three of the non-specific Kahn positive sera (after childbirth) were also positive by the rapid test.

The non-specific positive Meinicke sera were negative by the rapid test.

Kahn reaction and this finding indicates the sensitivity of the rapid test.

The above table shows the comparative results of this rapid test and other serological reactions.

SUMMARY

A simple rapid flocculation test for the serodiagnosis of syphilis is described.

The test is suitable for the examination of both serum and CSF.

The Rehabilitation of the Flavines

(From the *British Medical Journal*, Vol. I, 20th March, 1943, p. 355)

THE antiseptic treatment of wounds during the war of 1914-18 was generally considered a failure, and antiseptics has since then been commonly regarded as an outmoded method. That is not to say that it was ever totally abandoned, but persistence in its use has been due to habit and custom rather than to any conviction of its efficacy. Little has been expected of it, and in general little has been achieved by it. That this attitude has been abandoned and the antiseptic method restored in surgical estimation to a position far more secure than it ever held in the past is due in the first place to the discovery that sulphanilamide acts locally as well as systemically. To anyone who studied the work of Fildes and Woods on the action of sulphanilamide on the hæmolytic streptococcus it became abundantly plain that this compound is an antiseptic in every sense of the word: the nature of its action on bacteria is in fact the same as that of mercury perchloride. The difference between them is that sulphanilamide has a very low toxicity and can be maintained in adequate concentration and in free form throughout the body fluids, whereas mercury salts are highly poisonous to the body itself and cannot exist free because they combine with proteins. As soon as it was established that solid sulphanilamide is an efficient local preventive of infection, antiseptics regained repute, and minds were reopened to the possibilities of other agents for the same purpose. These others were both old and new, and among the new the astonishing properties of penicillin have attracted most attention, although the scarcity of supplies has so far prevented extensive clinical trial. Penicillin is suitable also for systemic use; another 'biological' antiseptic, gramicidin, is recommended only for local application, as is propamidine, to which we have referred recently.

Of the older antiseptics only the flavines have shared in this restoration to favour, a fact which has been no surprise to their few faithful advocates during the sequestered interwar period. The champion of these antiseptics since their earliest days, C. H. Browning, contributes at page 341 a restatement of their properties with an assessment of their position in the light of recent observations. It is noteworthy that the main facts, including the vital experimental evidence that acridine compounds will sterilize dangerously contaminated wounds, have been known for over twenty years. This work was done in part by Browning himself, by several workers in Germany, and by one in Japan, and taken together it forms an impressive bulk of evidence which has been inexplicably disregarded. Although these experiments have taken several forms, and employed various acridine compounds and different bacteria, they have regularly shown that these compounds will avert an otherwise fatal infection if applied to tissues into which virulent bacteria have recently been introduced. This could be said of no other antiseptic until the advent of the sulphonamides; indeed, control animals in some of these experiments were treated with such substances as phenol and mercury perchloride without effect. It has also been well known since their introduction that the flavines are comparatively non-toxic; they can be not only applied

to exposed tissues without causing evident damage but injected interstitially, this being the proper treatment of a dangerous punctured wound. Short of causing actual necrosis an antiseptic may admittedly do harm by damaging individual types of cell, and the toxicity of the flavines for leucocytes is the subject not only of a now historic controversy but of conflicting observations even within the past few years. So completely discordant are some of the results reported, that, as Browning says, they serve only to condemn some of the methods by which they were obtained. The weight of evidence on this point is that leucocytes will at least survive exposure to flavine concentrations which are bactericidal, even though their phagocytic capacity may be impaired.

It may well be asked why, if the flavines have these outstanding merits, their clinical performance has not been correspondingly successful throughout their twenty-six years' history. There are two answers to this question: wrong choice of compound and misapplication. The existence of three different acridines—apart from proprietary compounds such as rivanol and vuzine—popularly regarded as interchangeable, but in fact having quite different properties, has been an obstacle to successful use, particularly since acriflavine, the most popular, is now known to be the least satisfactory. A. Albert, who has synthesized a number of new acridine compounds, two of which are highly promising, drew attention five years ago to the superiority of proflavine, and this was strikingly illustrated by Russell and Falconer in their tests on the exposed rabbit's brain. The application and injection of solutions of acriflavine and various antiseptics of other kinds caused a severe hæmorrhagic necrosis, but a neutral isotonic solution of proflavine caused no more apparent damage than normal saline. Proflavine is therefore the compound of choice, and there is recent experimental evidence in the work both of Hawking and of McIntosh and Selbie that it is an efficient wound prophylactic; indeed, in the prevention of gas gangrene it appears to be superior to the sulphonamides. There is no corresponding evidence from the clinical field, because no organized attempt has been made to obtain it, whether in dealing with war wounds or otherwise. The new clinical evidence refers not to prevention but to the treatment of established infection, a totally different problem and one presenting greater difficulties. It is here that the method of application becomes most important, because it is clearly necessary that the antiseptic should not only penetrate every part of the wound but persist there in adequate concentration for a considerable period of time. Of the two chief methods used in the past neither was calculated to achieve this. The drawback of a wet dressing is that all the antiseptic dyes, including the acridines, have an affinity for fabrics, and tend rather to combine with them to diffuse away from them. The B.P.C. acriflavine emulsion—perhaps the commonest form in which any acridine compound has been used for twenty years past—is so constituted that almost none of the acriflavine can escape from it, and it is therefore of no more value than simple liquid paraffin. The solution to this problem, which proves to be simplicity itself, was found in Libya by Mitchell and Buttle, who introduced proflavine into wounds by the same method, though not in the same quantity, as sulphanilamide—namely, as a powder. The solubility of proflavine sulphate is about 1 in 300, and by analogy with what is known of the relation between solubility and persistence in wounds among the sulphonamides, it may be deduced that under given conditions a moderate amount of proflavine will take at least two days to undergo complete solution, and will therefore act in full concentration throughout that time. The results obtained by this treatment, even in cases of intractable suppuration, were often dramatic. These are good reasons for saying that the flavines have come into their own again; proflavine has indeed come into rather more than has ever been claimed in the past. It should certainly be given further trials in comparison with other agents for both prevention and treatment of wound infections.

Importance of the Rh Factor

(From the *Lancet*, Vol. I, 8th May, 1943; p. 587)

THE rhesus (Rh) factor in blood is of practical importance as well as academic interest. A circular¹ containing recommendations by a subcommittee of the Medical Research Council makes it clear that application of present knowledge of this factor would considerably reduce the number of serious hæmolytic reactions following transfusion and should much improve the treatment of hæmolytic anæmia of the newborn.

The red cells of the majority of human beings contain, irrespective of their ABO group, an agglutinin, Rh.² The designation Rh is used because a similar agglutinin is found in the red cells of the rhesus monkey, and the presence of the agglutinin in human red cells was first discovered by testing them against an anti-rhesus serum. Only about 15 per cent of people in this country lack the Rh agglutinin.³ In the case of the ABO groups, persons whose red cells lack the A or B agglutinins have the corresponding anti-A or anti-B agglutinins in their plasma. Persons whose red cells lack the Rh agglutinin (Rh-negative) do not normally have anti-Rh agglutinins in their plasma, but are liable to form them if Rh agglutinin is introduced into their circulation. It may be introduced in one of two ways: (1) in persons of both sexes, when Rh-positive blood (whose red cells contain the Rh agglutinin) is transferred,⁴ and (2) in women, after becoming pregnant with an Rh-positive foetus (the foetus having inherited the Rh agglutinin from the father). From the transfusion point of view, the importance of the presence of anti-Rh agglutinins, developed as a result of transfusion or of pregnancy, is that a subsequent transfusion of Rh-positive blood will prove incompatible. Since 85 per cent of bloods are Rh-positive, the chances of incompatible blood being given in such a case, when transfusion is required, are considerable unless Rh-negative blood (of suitable ABO group) is selected.

Apart from pregnancy, the development of anti-Rh agglutinins by Rh-negative persons usually occurs only after the repeated transfusion of Rh-positive blood, and as a rule it can then be suspected from the poor response to transfusion—e.g. failure of the hæmoglobin to rise satisfactorily, or the onset of jaundice or more serious signs of hæmolysis. The development of anti-Rh agglutinins by Rh-negative women during pregnancy is potentially more dangerous because the first evidence of it may be a serious hæmolytic reaction following a first transfusion.* A clue may, however, be provided by the obstetrical history. When anti-Rh agglutinins are formed in the plasma in response to the passage of the Rh agglutinin from the foetus across the placenta, the anti-Rh agglutinins pass back across the placenta into the foetal circulation and destroy some of the foetal erythrocytes.⁵ This hæmolysis is the central feature of the group of conditions known as erythroblastosis foetalis. The classical forms of this disease are well known: the infant may be born dead or moribund and exhibit universal oedema (hydrops foetalis); it may be born jaundiced or may develop severe jaundice within 48 hours of birth (icterus gravis neonatorum), or it may be normal at birth but develop severe anæmia within a few days (congenital anæmia of the newborn).

Some of the infants born dead, often before term, are outwardly normal, although pathological examination may reveal the true state of affairs. The term 'erythroblastosis' suggests that the formation of nucleated red cells is the essential feature of the disease, but Parsons and his colleagues⁶ have long maintained that the primary process is a destruction of the infant's red cells, that the erythroblastosis is merely a response to this destruction, and that the term 'hæmolytic anæmia of the newborn' should be used instead. An even better name would be 'hæmolytic disease of the newborn (or of the foetus)',⁷ because the infant may not be anæmic although its red cells are being destroyed at an abnormal rate. The disease in its various forms is not uncommon: its incidence has in fact been estimated at 1 in 400 pregnancies.⁸

Hæmolytic disease of the newborn should not, of course, be confused with hæmorrhagic disease of the newborn, a condition attributable to deficiency of prothrombin and curable by intramuscular injection of adult blood or by injection of vitamin K. Hæmolytic disease of the newborn should be treated by the intravenous transfusion of Rh-negative blood;⁹ such blood survives for long periods in the circulation of affected infants, whereas Rh-positive blood is usually rapidly destroyed.¹⁰

Anti-Rh agglutinins, unlike the ordinary anti-A and anti-B agglutinins, are 'immune bodies' and therefore increase at first in strength, then decrease and finally disappear. They may persist, however, for at least 5 years,¹¹ and sensitivity to the Rh agglutinin may last even longer. If there has been evidence of hæmolytic disease in any infant—past or present—one must presume that anti-Rh agglutinins are present in the mother's blood and that transfusion will be extremely dangerous for her unless the blood comes from an Rh-negative donor of suitable group. This should be a useful safeguard; but, unfortunately, while an infant remains *in utero* there may be nothing to suggest that it has hæmolytic disease. Again, if an Rh-negative woman receives repeated transfusions of Rh-positive blood, she may form anti-Rh agglutinins so that in her next pregnancy her infant develops hæmolytic disease.¹² One must look forward, therefore, to the time when Rh-negative women will be detected at the antenatal clinic, so that if they have to be transfused they will be given Rh-negative blood. For the time being, it would be a substantial advance if no mother whose present or previous infant has shown signs of hæmolytic disease were transfused except with Rh-negative blood of suitable ABO group. Actually the Rh factor is not responsible for quite all cases of hæmolytic disease of the foetus, but only for some 92-94 per cent.¹³ Where the foetal erythrocytes contain A or B agglutinins and the mother's erythrocytes lack them, the foetal cells may be destroyed by anti-A or anti-B agglutinins; while in other cases rare blood-group factors, present in the foetal erythrocytes but not in the maternal erythrocytes, may be concerned. These facts have to be appreciated if clinicians are to interpret correctly the results of laboratory tests in suspected cases of hæmolytic disease of the newborn.

It is not easy to get reliable results when making tests for Rh agglutinogens and anti-Rh agglutinins. The reactions are weaker than the ordinary isoagglutination reactions, and can be detected only by the use of a tube technique; they are almost always stronger at 37°C. than at room temperature. The serum may have to be titrated against the cells to show any reaction,¹⁴ and different sera do not give parallel reactions,^{15,16} probably because there are

* On another page practitioners are invited to help by reporting promptly any such accidents.

¹ The danger of hæmolytic transfusion reactions due to immunization of the recipient to the Rh factor. Ministry of Health Circular (EMSI 413).

² Landsteiner, K., and Wiener, A. S. *J. Exp. Med.*, 1941, **74**, 309.

³ Boorman, K. E., Dodd, B. E., and Mollison, P. L. *Brit. Med. J.*, 1942, *ii*, 535 and 569.

⁴ Wiener, A. S., and Peters, H. R. *Ann. Intern. Med.*, 1940, **13**, 2306.

⁵ Levine, P., Katzin, E. M., Burnham, L., and Vogel, P. *Amer. J. Obstet. Gynec.*, 1941, **42**, 925.

⁶ Parsons, L. G., Hawksley, J. C., and Gittins, R. T. *Arch. Dis. Childh.*, 1933, **8**, 159.

⁷ Levy, H. *Brit. Med. J.*, 1942, *ii*, 738.

⁸ Javert, C. T. *Surg. Gynec. Obstet.*, 1942, **74**, 1.

⁹ Mollison, P. L. *Proc. R. Soc. Med.*, 1943, **36**, 5, 221.

¹⁰ Diamond, L. K. *New Eng. J. Med.*, 1942, **227**, 857.

¹¹ Taylor, G. L., Race, R. R., Prior, A. M., and Ikin, E. W. *Brit. Med. J.*, 1942, *ii*, 572.

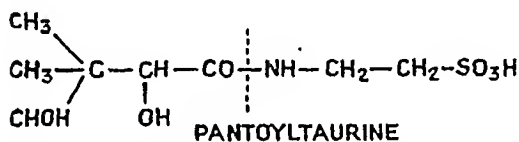
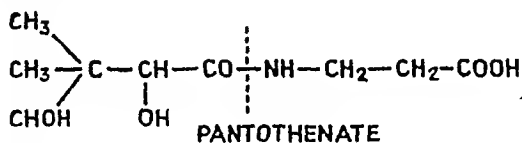
different kinds of Rh agglutinogens and anti-Rh agglutinins. Hence it seems likely that the tests should at present be left to blood transfusion centres and other special laboratories. But these centres need the help of clinicians in maintaining stocks of suitable sera, which are most easily obtained from immunized women. They can do it only if clinicians will have their cases tested and then persuade women with strong anti-Rh agglutinins to give some of their blood for the preparation of test sera.

Antibacterial Strategy

(From the *Lancet*, Vol. I, 10th May, 1943, p. 463)

MANY important discoveries are the result of an accident which the genius of an investigator has turned to good account. The discovery of penicillin by Fleming is an example, and in a different way the sulphonamides owe their being to a series of such accidents. The Germans tried prontosil in the hope that here would be just another antiseptic dyestuff with a greater affinity for bacteria; by chance they were opening up a new and priceless field in the treatment of disease. In looking for coal they had stumbled on a gold mine. They put the sulphonamide group into their dyes to make them stain better; the therapeutic activity of prontosil however was due, not to its staining properties, but to the happy chance that the human body could reduce azo dyes—the reduction product had a fatal attraction for bacteria which preferred it to their proper food. And still the luck held. Prontosil is so weakly active that it would have been pronounced inactive against almost any other organism than the hæmolytic streptococci against which it was tested. Time has gone by and other more potent drugs have replaced prontosil and sulphanilamide. These have been produced by the routine work of chemists highly skilled at complicated substitutions. The products were tested and the results sifted until out of hundreds of compounds sulphapyridine, sulphathiazole and sulphadiazine have emerged as the most useful.

In our opening page McIlwain and Hawking describe possibly the first case of successful chemotherapy in which every step had been planned beforehand. Pantoyltaurine is not a sulphanilamide or a penicillin from the point of view of effectiveness, but unlike them it is not a chance discovery. It was known that pantothenic acid was an essential factor for the growth of



hæmolytic streptococcus, and a compound was devised which by analogy with sulphanilamide should limit growth by competing with the natural factor. McIlwain determined the ratio of pantoyltaurine to pantothenic acid necessary to secure inhibition of growth of the bacteria *in vitro*, and he estimated the blood content of pantothenic acid in the rat; the dosage of pantoyltaurine was then arranged so as to produce the inhibitory concentration of the drug in animal's blood over a period of time. Doses giving this level saved the animals, and smaller doses did not, which brilliantly supports the theories on which the treatment was based.

The era of chance in chemotherapy is not over. Our knowledge of bacterial and virus metabolism is painfully meagre and the lucky chance skilfully taken

will continue to play a leading part in advances in this field. But progress will come more and more from planned experiments in which theory precedes achievement. Biochemistry seems the best weapon to achieve this, and has indeed been in a position for many years to give help in chemotherapy. Examples of interference with synthetic processes by drugs which poisoned the enzyme, or which being similar to the natural substrate combined with the enzyme and inhibited the synthesis, have been known for a long time. But Ehrlich's concept of chemotherapy, which exercised so great an influence, was essentially chemical, and having no connection with nutrition divorced chemotherapy from biochemistry. The credit for formulating the concept of drugs which could limit growth by competing with essential metabolites rests with Fildes and his school. The concept is delightfully simple. The growth of bacteria depends on the synthesis of complex substances from simple compounds, and on reactions which can supply the necessary energy for these syntheses. All along this synthetic path are essential substances, and any interference with their supply or use limits growth. The task of the chemotherapist is to discover these substances and then to inactivate them, or to devise counterfeit compounds which the organism will accept and too late find useless for its purpose. This view regards the animal host as a culture medium for bacterium or virus, which is what essentially it is, and points the way to further advances through biochemical investigation of bacterial and virus metabolism.

Chemotherapy by Blocking Bacterial Nutrients

By HENRY McILWAIN, M.Sc., Ph.D.

and

FRANK HAWKING, D.M.

(Abstracted from the *Lancet*, Vol. I, 10th April, 1943, p. 449)

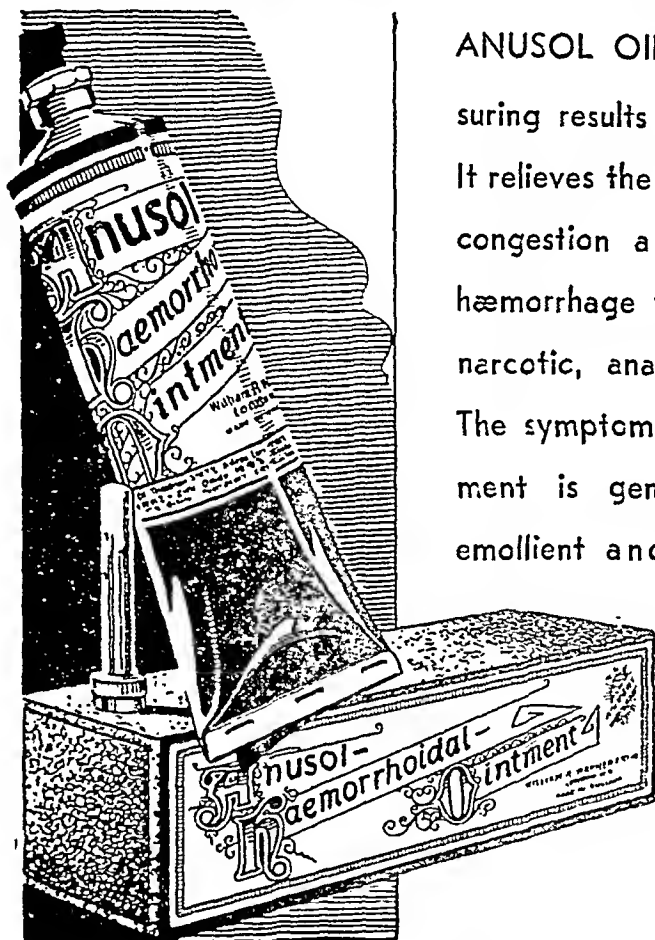
MANY bacteria need for their growth small amounts of vitamin-like substances, and pathogenic organisms obtain some of these from their host. Pantoyltaurine is a compound which was designed to inhibit growth of bacteria needing pantothenate, a substance of this type, by displacing it from the points at which it interacted with micro-organisms and so in effect starving them of a substance essential for growth. *Strep. hæmolyticus* was particularly sensitive to this action *in vitro*, and its growth was retarded when the ratio of pantoyltaurine to pantothenate concentrations was above a certain range. Natural materials (e.g. blood and animal extracts) contained little material other than pantothenate which interfered with the action of pantoyltaurine, so that the concentrations at which the drug should starve streptococci of the hosts' pantothenate could be judged from the concentration of that substance in the animal.

Pantoyltaurine was rapidly excreted by rats, but the ratio of pantoyltaurine to pantothenate concentrations in their blood could be kept above the range of *in vitro* action for most of the day by frequent subcutaneous doses, to which there was no intolerance. Rats so treated for 4 days were protected from approximately 10,000 LD of a virulent strain of streptococcus (Richards), and less completely from 1,000,000 LD. Lower dosage did not afford protection. Similarly mice, whose blood pantothenate was much higher than those of the rat or of man, were not protected. The validity of this deduction of *in vivo* action from *in vitro* experiments was confirmed by artificially raising the blood pantothenate of rats, when the previously effective dosage of pantoyltaurine became ineffective.

Sulphonamide-resistant streptococci and some strains of *C. diphtheriae* are sensitive to pantoyltaurine. Since the concentration of pantothenate in human blood is

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slightly less than that in rat blood, somewhat lower levels would be necessary for therapeutic action in man. Practical applications to human therapy may be possible along these lines, but the main value of this work lies in its description of new methods for the discovery of chemotherapeutic compounds.

Sterilization of Sulphonamides

By J. E. McCARTNEY

and

R. CRUICKSHANK

(Abstracted from the *Lancet*, Vol. II, 17th October, 1942, p. 454)

A RECENT report of a case of tetanus associated with the local application of a sulphonamide powder has impressed upon British hospital authorities the need for issuing sulphonamide compounds for local application in a sterile form and in a sterile container. Tests which the present authors have made, working in the London County Council Hospital Service, show that sulphonamide powders often contain sporing organisms and that the cardboard containers in which the powders are supplied may be heavily infected with sporing organisms including *Clostridium welchii*. They have by a simple procedure been able to issue sterilized preparations of the three common sulphonamides (sulphanilamide, sulphapyridine and sulphathiazole) in a sterile usable container without any apparent physical or chemical change in the powders.

TECHNIQUE OF STERILIZATION

Wide-mouthed screw-capped containers of 1 ounce (28 cm.³) capacity fitted with aluminium caps tightly screwed on, and red rubber washers, are sterilized in the autoclave at 15 lb. (6.8 kg.) for 20 minutes. The sulphonamide powder is obtained from the manufacturers in clean screw-capped glass jars, and not in cardboard containers. The assistant who fills the bottles washes up as for a surgical dressing. A sheet of sterile paper is placed on the bench, and, with a sterilized teaspoon and a 3-inch (7.6 cm.) glass funnel cut off at the neck, the sulphonamide powder is placed in the previous sterilized containers. The powder is shaken down until the bottle is nearly full (approximately 10 grammes) and the cap is then screwed tightly on. When the batch is ready the bottles are placed in the autoclave and heated with the steam issuing freely for 20 minutes. The pressure is then raised to 10 lb. (4.5 kg.) and allowed to act for 30 to 60 minutes.

The rationale of the process is that, although the powder is in a tightly closed container, sterilization is by moist heat because the powder normally contains 0.2 to 0.5 per cent of water which in 10 g. of material is 0.02 to 0.05 cm.³ water. The water vapourizes and permeates the powder completely as steam, being reabsorbed when the bottles cool down. The powder does not cake because there is no addition of moisture, while the comparatively low temperature of 116°C. does not alter the colour. If the powder is dried in the hot-air oven at 145-160°C. the moisture is evaporated, and the heat penetrates only by conduction from one granule of powder to another. Moreover organisms are much more resistant to dry heat than to moist heat, so that heating must be prolonged for 3 to 4 hours. The method of autoclaving therefore kills the contaminating organisms more easily, quickly, and at a much lower temperature and avoids physical or chemical alteration of the powder.

In many hospital sterilizers, sterilization at a pressure of 10 lb. is not very convenient since the valves are set to give higher pressures—15 to 20 lb. The sulphonamide powders may be sterilized at this higher pressure by the procedure outlined above without

apparent detriment, except that there may be slight yellowish discoloration. At a pressure of 15 to 20 lb. for 20 to 30 minutes cultures of bacillus subtilis spores dried on lint, enclosed in paper and placed at the bottom or in the middle of the container are invariably killed. At the lower pressure of 10 lb. for 1 hour, *B. subtilis* spores are also killed; at 10 lb. for half hour not uniformly so.

A further advantage of the use of the screw-capped bottle is that when the cap is removed the whole top and lip of the bottle is sterile, having been covered by the screw-cap, and the powder can be poured out of the bottle directly on the wound without fear of contamination. Alternatively a perforated cap may be used which acts as a sprinkler.

The authors conclude by recommending a procedure to be adopted for the use of the sterilized containers in the operating theatre.

Sulphonamide Sunlight Eruptions—A Clinical Study of 27 Cases

By R. G. PARK

and

W. M. PLATT'S

(Abstracted from the *British Medical Journal*, Vol. II, 12th September, 1942, p. 308)

THE constant sunshine of the Middle East and the presence of ambulant military cases of venereal disease undergoing chemotherapy give unusual opportunities for the study of sulphonamide photodermatitis, which was first noted by Newman and Sharlit (1937).

The authors of the present paper are both medical officers serving with the New Zealand Medical Corps; and they describe 27 cases of light-sensitive sulphonamide eruption, 21 due to sulphanilamide and 6 to sulphapyridine. These represent 3.4 per cent of the total cases treated with these drugs, under conditions favouring considerable exposure to constant strong sunlight. About half the cases occurred during July and August.

Photosensitization of the skin occurred from the eighth to the tenth day of administration. Two cases were found to be photosensitive 2 days after stopping chemotherapy. It therefore appears that patients given sulphonamides for more than 6 days are possible victims of sunlight eruptions.

In many cases the presence of melanin appeared to be a protection against these eruptions. These observations support this view: (1) about one-third of the cases were subjects susceptible to sunburn; (2) the bronzed parts of the body tend to be affected less than the others; (3) no eruptions have ever been seen in Maoris, who comprised about 100 of the 800 cases treated during the 12 months.

The parts were affected in the following order of severity: (a) parts exposed to the sun during chemotherapy; (b) parts exposed in the past; (c) pressure points, such as the great trochanters; (d) least of all, parts always kept covered, such as the bathing-drawers area.

The commonest lesions were erythematous papules in a morbiliform or roseoliform pattern, becoming confluent. Itching varied (severe in 5, moderate in 7, slight in 9, absent in 6). Less common lesions were oedema, urticaria, vesication, pustulation, and desquamation.

Drug fever and other toxic effects were common accompaniments (12 cases).

Most rashes subsided within 2 to 4 days.

REFERENCE

- NEWMAN, B. A., and J. *Amer. Med. Assoc.*, 109, SHARLIT, H. (1937). 1036.

Paratyphoid Carriers: The Infectivity of the Faeces and the Failure of Chemotherapy with Sulphapyridine and Iodophthalein

By H. D. HOLT
and
H. D. WRIGHT

(Abstracted from *Bulletin of Hygiene*, Vol. XVII, p. 655, in *Journal of Pathology and Bacteriology*, Vol. LIV, April 1942, p. 247)

FÆCAL specimens, taken without any particular precautions to ensure liquid stools or to preserve the specimen during transmission, were examined at frequent intervals from one chronic carrier of *Bact. paratyphosum B* of five years' duration and 13 persons who had been excreting the organism for 6 months or more. The method used consisted in enrichment in tetrathionate broth and plating on Wilson and Blair's medium or brilliant green-eosin-agar. Very few negative results were obtained and it is concluded that much of what passes for intermittency has been due to inadequate technique for the isolation of small numbers of the pathogen from large numbers of *Bact. coli*.

Data on the numbers of pathogens in the faeces of carriers are, however, lacking, and the authors collected evidence on this point by making serial dilutions of faeces in broth and determining the relative numbers of *Bact. coli* and *Bact. paratyphosum B* by plating the broths on MacConkey agar after incubation and tetrathionate broths, inoculated from the dilutions, on Wilson and Blair's medium. It was found that in general the number of pathogens was very large and was consistently maintained. Sometimes the pathogen was in excess, in other cases there was only one pathogen to a million *Bact. coli*, but more often the ratio was 100 to 1,000, *Bact. coli* to one *Bact. paratyphosum B*. Without adequate enrichment media therefore a false negative might easily be obtained.

The authors also record the failure of soluble iodophthalein in 10 trials and of sulphapyridine in 7 trials to influence the carrier state. One carrier cleared suddenly and permanently two days before treatment started, a result which illustrates how readily false conclusions might be drawn from individual cases.

(Abstract adapted from *Bulletin of Hygiene*, 17, 655, September 1942.)

Journal of the Malaria Institute of India

December 1942, 4, pp. 429-634

- ON a New Variety of *Anopheles turkhudi* from Palestine, by Z. Saliternik and O. Theodor, p. 429.
- * Studies on Malaria in the Deltaic Region of Bengal, by M. O. T. Iyengar, p. 435.
- A New Variation of *Anopheles gambiae*, by B. de Burca and M. Yusuf, p. 447.
- Notes on the Mosquito Fauna of Rot-holes in Trees and Bamboo Stumps in Ceylon, by D. P. Wijesundara, p. 451.
- * Malaria in the Coastal Belt of Orissa, by G. Covell and Pritam Singh, p. 457.
- * Studies on the Behaviour of *Anopheles minimus*. Part VII. Further Studies on the Composition of the Water in Breeding Places and the Influence of Organic Pollution, by R. C. M. Thomson, p. 595.
- * Studies on the Behaviour of *Anopheles minimus*. Part VIII. The Naturalistic Control of *A. minimus* in Shallow Earth Wells, by R. C. M. Thomson, p. 611.
- * A Demonstration Project in the Control of Rural Irrigation Malaria by Antilarval Measures, by F. W. Knipe and P. F. Russell, p. 615.
- * Observations on the Relative Utility of *Gambusia affinis* and *Panchax parvus* in the Control of Mosquito Breeding in Wells and Tanks, by R. B. Rao and H. Ramoo (Abstract), p. 633.
- (Of papers marked * the author's summary is given here.)

STUDIES ON MALARIA IN THE DELTAIC REGION OF BENGAL

1. In the deltaic region of Bengal, contrary to conditions prevailing in other regions, areas with a high subsoil water level during the wet season are comparatively free from malaria, while those with a low subsoil water level show a high incidence of the disease. The factors that would account for the malariousness of dry areas and the healthiness of wet areas have hitherto not been clearly understood.

2. In order to study the factors that determine malarial endemicity in this region, a series of observations were carried out in a group of villages with different spleen rates. The local malaria vector was shown to be *A. philippinensis*. This species has been found infected in different parts of deltaic Bengal, often with high infection rates.

3. A high prevalence of *A. philippinensis* is associated with a high malarial incidence, and a low prevalence of the mosquito with a low malarial incidence. The prevalence of *A. philippinensis* shows a significant positive correlation with the spleen rate.

4. The main breeding season of *A. philippinensis* is from July to October. The depth of the water table below the ground surface during the breeding season of *A. philippinensis* appears to have a marked influence on the prevalence of this species. In villages with a low water table the density of *A. philippinensis* was high. In villages where the water table was close to the ground surface the incidence of this mosquito was very low. A significant positive correlation was observed between the density of *A. philippinensis* and the distance of the water table from the ground level during the wet season.

MALARIA IN THE COASTAL BELT OF ORISSA

1. Investigations regarding malaria conditions in the coastal belt of Orissa Province were carried out during the period April 1939 to March 1942. Detailed routine observations were made in the area extending from Chatrapur, 16 miles south of Chilka Lake, to Sana Nairi, half-way along its western margin, throughout this period, and special expeditions to investigate particular problems were made to a number of other villages in the vicinity of the lake and in the coastal belt as far south as Vizianagram.

2. The distribution of malaria in this area is patchy and irregular. Hyperendemic conditions prevail in certain villages, and epidemics of a serious nature occur from time to time either in the spring or autumn months.

3. The malaria vector throughout the region is *A. sudaicus*. There is no evidence that any other species plays any part in the transmission of the disease.

4. *A. sudaicus* breeds in Chilka Lake itself when conditions are favourable, and also in tanks, pools, swamps and ricefields subject to flooding by saline water.

5. The furthest distance inland at which *A. sudaicus* was found was 6 miles from the shore of Chilka Lake. The most southern point at which it was found was at Bavanapada, 81 miles south of the Chilka Lake.

6. The bearing of the investigations made in recent years on the validity of certain earlier records regarding the distribution of *A. sudaicus* is discussed.

7. The chief factor favouring the breeding of *A. sudaicus* is the presence of putrefying algae and other weeds. The optimum range of salinity in this area is from 600 to 800 parts per 100,000, but salinity probably only operates in so far as it affects the growth of the weeds.

8. Removal of weeds from breeding places is followed by a cessation of breeding of *A. sudaicus*. Experiments carried out in certain villages indicate that this is the most promising method of controlling malaria in the Orissa coastal belt.

9. The spray-killing of adult mosquitoes with pyrethrum insecticide is recommended as the most effective emergency measure to deal with epidemics of malaria in this area.

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STUDIES ON THE BEHAVIOUR OF *Anopheles minimus*

PART VII

1. Previous studies on the dissolved organic matter of the water, and its influence on the behaviour of *A. minimus* have been extended to a study of oviposition in the field.

2. By means of an additional analytical method (the oxygen absorbed from alkaline permanganate) some information about the quality of the organic matter has been obtained.

3. Analysis of water in earth wells and egg pits has given further information as to the composition of water in which the eggs are actually laid in nature.

4. It is suggested tentatively that the point at which organic content of the water becomes a limiting factor in oviposition is represented approximately by the following composition :—

Oxygen absorbed from acid permanganate (Tidy's figure) in 4 hours at 40°C.	6.0 parts per million
Oxygen absorbed from alkaline permanganate	12.0 " " "
Albuminoid ammonia	1.0 part " "
'Degree of pollution'	8.0
Ratio $\frac{\text{alkaline permanganate figure}}{\text{acid permanganate figure}}$	2.0

An organic content which gives a higher figure than the first four of these estimates, or a ratio $\frac{\text{alkaline permanganate figure}}{\text{acid permanganate figure}}$ less than 2.0, is probably sufficient in itself to repel the female mosquito from an otherwise suitable breeding place.

5. Field experiments confirm and extend previous conclusions about the influence of organic matter on the selection of the breeding place. The organic content of the water in many stagnant ricefields, and in some tanks and borrowpits at certain times of the year, is sufficiently high in itself to explain the continuous absence of *A. minimus*. But many other ricefields and collections of stagnant water similarly avoided by *A. minimus* have an organic content well within the range tolerated by the female mosquito.

6. The water in heavily shaded pools under Tarapat (a 'shade' plant) shows the following characteristics with regard to dissolved organic matter :—A low or moderate figure for acid and alkaline permanganate titrations, and for albuminoid ammonia, coupled with a low ratio $\frac{\text{alkaline permanganate figure}}{\text{acid permanganate figure}}$ and an unusually low figure for dissolved oxygen. In some pools, dissolved oxygen is practically absent and as such may possibly be a limiting factor in this case.

STUDIES ON THE BEHAVIOUR OF *Anopheles minimus*

PART VIII

A simple method of controlling the breeding of *A. minimus* in shallow 'kachcha' wells is described. It depends on the fact that *A. minimus* will not oviposit along a bare edge which is fully exposed to light. By removing all vegetation from the water edge, and converting vertical earth walls into smooth sloping ones, almost perfect control is brought about. As there is no interference with the water itself, the method is particularly useful in wells used for drinking purposes.

A DEMONSTRATION PROJECT IN THE CONTROL OF RURAL IRRIGATION MALARIA BY ANTILARVAL MEASURES

An experiment is reported on the control of irrigation malaria in an area of 7 square miles in South India, by antilarval measures, including some 55,000 cubic yards of filling, draining, use of *Gambusia*, of chopped cactus, of paris green and of intermittent irrigation. The programme, extended over a period of four years, affected a population of some 3,390 persons in a strictly rural area, and cost Rs. 4-6-0 (\$1.31 or £0-6-6) per capita. Maintenance costs during one year of observation

after completion of the engineering measures were only Re. 0-1-11 per capita (\$0.34 or £0-0-24).

The control measures resulted in a notable fall in spleen and parasite rates.

OBSERVATIONS ON THE RELATIVE UTILITY OF *Gambusia affinis* AND *Panchax parvus* IN THE CONTROL OF MOSQUITO BREEDING IN WELLS AND TANKS

A series of experiments was carried out at Pattukkottai, Tanjore District, Madras Presidency, to test the relative efficacy of *Gambusia affinis*, an American fish which has been acclimatized in India for the last 12 years, and of *Panchax parvus*, a local indigenous species, in the control of mosquito breeding. As the result of observations made both in the laboratory and in the field, the following conclusions were reached :—

1. *Gambusia affinis* is more adaptable to diverse environmental conditions than *Panchax parvus*, which thrives best in natural surroundings and is not suited for use in confined waters.

2. *Gambusia affinis* thrives better than *Panchax parvus* in wells and is more effective for controlling mosquito breeding in them.

3. *Gambusia affinis* is easier to rear in large numbers in artificial hatcheries than *Panchax parvus*.

4. *Gambusia affinis* devours more larvae and at a quicker rate than *Panchax parvus*.

The authors consider that *Gambusia affinis* has proved of great utility in the control of mosquito breeding in Pattukkottai, both in wells and in tanks.

Indian Journal of Medical Research

May 1943, 31, pp. 1-123

- * Coliform Organisms from the Urinary Tract, by N. Seshadrinathan and S. Venkataswami, p. 1.
- * The Action of Dyes on Vibrios, by G. Panja and S. K. Ghosh, p. 5.
- * Studies in Fish-Liver Oils. Part I. The Biological Assay of Vitamins A and D in Ghol- (*Sciama miles*) and Mushi- (*Scoliodon sorokowah*) Liver Oils, by S. P. Niyogi, V. N. Patwardhan and B. N. Acharya, p. 15.
- * Studies in Fish-Liver Oils. Part II. The Seasonal Variation in the Yield and Vitamin-A Content of some Fish-Liver Oils, by S. P. Niyogi, V. N. Patwardhan and B. N. Acharya, p. 21.
- * Investigations on the Food Value of Fish and other Marine Products. Part II. The Protein and Mineral Contents, by M. L. Khorana, M. L. Sarma, P. Seshagiri Rao and K. V. Giri, p. 25.
- * Availability of Calcium in Lady's Finger (*Hibiscus esculentus*), Cabbage (*Brassica Oleracea capitata*), Drumstick (*Moringa Oleifera*) and Amaranth Tender (*Amaranthus gangeticus*). Part I. Availability of Calcium in Vegetables determined by Experiments on Growing Rats, by K. P. Basu and D. Ghosh, p. 29.
- * Availability of Calcium in Lady's Finger (*Hibiscus esculentus*), Cabbage (*Brassica Oleracea capitata*), Drumstick (*Moringa Oleifera*) and Amaranth Tender (*Amaranthus gangeticus*). Part II. Availability of Calcium in Vegetables determined by Metabolism Experiments on a Human Adult, by K. P. Basu and D. Ghosh, p. 37.
- The Determination by Chemical Methods of the Food Values of yet another Batch of Edibles, by K. Mitra and H. C. Mittra, p. 41.
- * Determination of the Biological Value of Proteins from Red Ants (*Ecophylla smaragdina*) by the Balance-sheet Method, by K. Mitra and H. C. Mittra, p. 45.
- * Nutrition and Its Bearing on Preventable Blindness and Eye Diseases in Bengal, by E. O'G. Kirwan, K. Sen and N. Bose, p. 49.
- * *Luffa acutangula*: The Chemical and Pharmacological Investigation of *Luffa* Seeds, by K. S. Grewal and B. D. Kochhar, p. 63.

- * The Pharmacological Action on the Circulatory System of a Bitter Principle isolated from *Securigera securidaca* (Linn.) Dagen et Dörfler (N. O. Leguminosæ), by P. De, p. 67.
 - * Hypnotic Effect of *Rauwolfia serpentina*: The Principle underlying this Action, Its Probable Nature, by R. N. Chopra, J. C. Gupta, B. C. Bose and I. C. Chopra, p. 71.
 - * Studies in Hæmolysis: With 'Histological Notes' by N. V. Bhaduri and 'Statistical Analysis' by C. Chandra Sekar, by L. E. Napier and P. C. Sen Gupta, p. 75.
 - * On the Fragility of Erythrocytes. Part I. In Hypotonic Saline, by A. C. Roy, p. 103.
 - * Surface Tension and Hæmolysis, by A. C. Roy, p. 109.
 - Variability in Rates of Population Change, with Reference to India, 1881 to 1931, and 1941: Some Statistical Consideration, by A. Geddes, p. 115.
- (Of papers marked * the author's summary is given here.)

Coliform ORGANISMS FROM THE URINARY TRACT

A study of 72 strains of coliform bacteria isolated from infections of the urinary tract showed that typical aerogenes forms were present in about 30 per cent, and typical coli organisms in about 35 per cent of cases. Intermediates accounted for 18 per cent, while the rest could not be grouped. This finding is in agreement with that of other workers in England and America.

THE ACTION OF DYES ON VIBRIOS

1. Brilliant green (1 in 100,000) exerts a bacteriostatic effect on Inaba and Ogawa sub-types of *V. cholerae*. El Tor vibrio and the Basra strain of non-agglutinating vibrio. Crystal violet and methylene violet (each 1 in 100,000), malachite green, acriflavin, gentian violet, methyl violet, methylene blue, fluorescein, pyronin yellowish (each 1 in 50,000), thionin (1 in 25,000), mercurochrome, safranin and basic fuchsin (each 1 in 5,000) exert the same inhibitory effect on the above vibrios. Eosin, methyl red, neutral red, borax carmine, indigo carmine, alizarin, aniline blue and nigrosin (each 1 in 5,000) do not inhibit the vibrios. Red dyes have poor bacteriostatic effect on vibrios.

2. Brilliant green and malachite green dyes (1 in 100,000) exert a complete selective bactericidal effect on most Inaba and Ogawa sub-types of *V. cholerae* and on large numbers of para-cholera vibrios isolated from clinical cholera cases but are harmless to non-agglutinating vibrios isolated from Hooghly water.

3. The few dye-resistant strains of *V. cholerae* that were tested were not found rough.

4. Dye-sensitivity and pathogenicity to laboratory animals were not found uniformly correlated. As a rule dye-sensitive strains were found more commonly and early invasive.

5. Organisms belonging to the genera—*Bacterium*, including *salmonella* and *shigella*, *proteus*, *pyocyanica*, *staphylococcus*, *streptococcus*, and *subtilis* group are not affected by the same concentrations of green dyes.

6. Acriflavin, crystal violet, gentian violet (1 in 100,000) fail to exert the bactericidal effect on Inaba and Ogawa sub-types of vibrio cultures in nutrient broth.

7. As a rule persistence of green colour and clearing of turbidity after contact with the organisms indicate sterility and discharge of colour and presence of turbidity signify multiplication.

8. The presence of an excess of alkali in the medium prevents the bactericidal action of the green dyes.

9. The green dyes (brilliant and malachite) are non-toxic to man and laboratory animals in the doses employed.

10. Brilliant green added to cholera stools in a final dilution of 1/5,000, kills the vibrios in the stools. Thirty-five cases of cholera were treated with the dye per mouth. Vibrios in the stools disappeared earlier than in the untreated cases, but the clinical improvement was not marked as a rule, due probably to in-activation of the dye by alkaline intestinal contents.

STUDIES IN FISH-LIVER OILS. PART I

The liver oils from the two fish, viz, mushi (*Scoliodon sorrokowah*) and ghol (*Sciæna miles*), were subjected to the tintometric and biological methods of assay for vitamin A. The factor used to convert the blue values (as read) to I. U. was 4.2 (Bomskov, 1935). The two methods gave values which agreed in the case of mushi-liver oil. The biologically obtained value for ghol-liver oil was, however, considerably lower than that given by the tintometric method.

The vitamin-D content of these two liver oils determined by the bone-ash method was 97 I. U. and 575 I. U. per g. of oil for mushi- and ghol-liver oils respectively.

STUDIES IN FISH-LIVER OILS. PART II

The seasonal variation in the yield of the oil and the vitamin-A content of liver oils, of four varieties of fish, viz, mushi, wagli, shengti and ghol, has been studied.

The yield of the oils from the livers varied from month to month, in the case of each fish. The vitamin-A content also showed large variations. There was no definite relation between the yield of the oil and its vitamin-A content in the case of mushi- and wagli-liver oils; but in the case of shengti and ghol, the vitamin-A concentration was found to increase as the yield of the oil decreased. The relation between the two is given by the expression $\text{vitamin A} = K \log P + C$ where P is the per cent yield and K and C are constants which are different for the two oils.

INVESTIGATIONS ON THE FOOD VALUE OF FISH AND OTHER MARINE PRODUCTS. PART II

The protein and mineral contents of a number of economically important food fishes in the Northern Circars have been determined. The protein content ranges from 19 to 23 per cent; Ca, 0.006 to 0.090 per cent; phosphorus, 0.150 to 0.350 per cent; iron, 0.6 mg. to 2.5 mg. per cent and copper 0.01 mg. to 0.24 mg. per cent. The values indicate that these fish constitute a good source of protein, phosphorus and iron.

AVAILABILITY OF CALCIUM IN LADY'S FINGER. PART I

Healthy young rats, 4-week old, were placed on four diets in one of which all the calcium was supplied entirely by skimmed milk. In the case of two other diets the milk was entirely replaced by enough finely ground dried cabbage or lady's finger to provide the same amount of calcium and in the fourth, half of the skimmed milk was replaced by enough ground dried drumstick to provide the same amount of calcium as in the milk diet. At 8 weeks of age the animals were killed and their bodies analysed for calcium.

Comparison of the availability of calcium in these vegetables with that of milk was made by calculating for each an utilization factor which is the ratio of calcium retention to intake. The values for males were 0.87 for milk diet, 0.71 for lady's finger, 0.82 for cabbage and 0.70 for drumstick diet. The values for females were respectively 0.84, 0.70, 0.81 and 0.69. Sex difference was, therefore, practically without any appreciable effect on the utilization. The calcium of cabbage was almost as well utilized as that of milk. The calcium from the other two vegetables, namely lady's finger and drumstick, was also fairly available. The rats refused to take the amaranth diet.

AVAILABILITY OF CALCIUM IN LADY'S FINGER. PART II

Calcium metabolism experiments were conducted on a healthy adult to find whether the calcium in lady's finger, cabbage, drumstick and amaranth (leaves and tender stems) could be utilized to maintain the calcium equilibrium in human adults. These vegetables were given as supplement to two types of basal diets representing the typical Indian diets—one containing rice and fish and the other purely vegetarian. All the vegetables had a favourable effect on calcium balance and brought the Ca : P ratio to more favourable values. Amaranth in spite of its high oxalate content, served as a fairly good available source of calcium.

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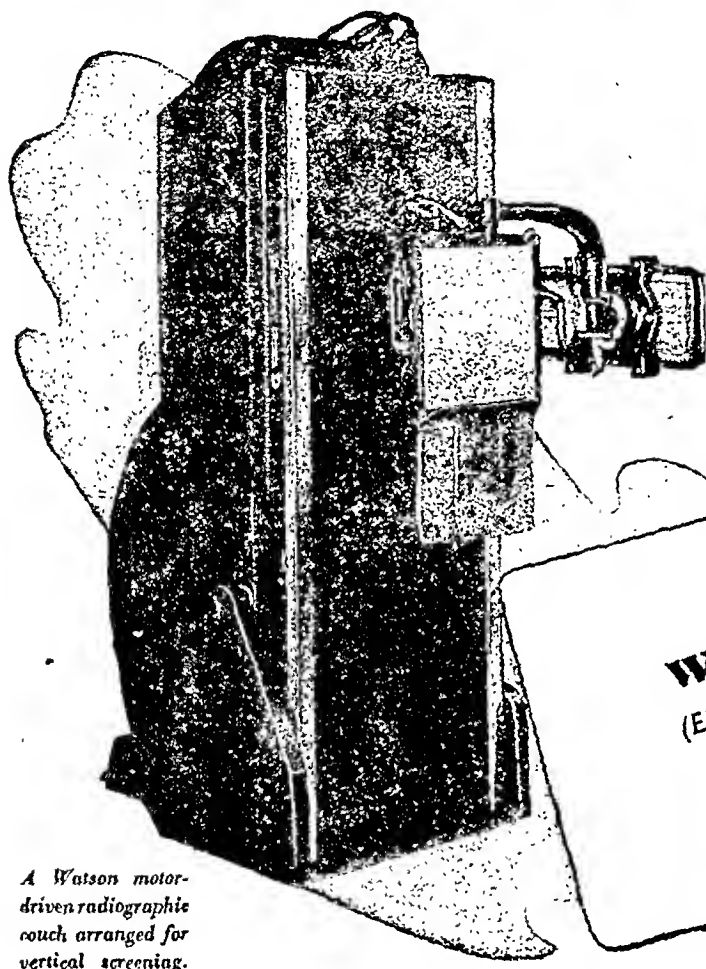
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Comparison with milk showed that except in the case of amaranth the utilization of calcium in the vegetables was much lower than that of the calcium in milk.

DETERMINATION OF THE BIOLOGICAL VALUE OF PROTEINS FROM RED ANTS (*Ecophylla smaragdina*) BY THE BALANCE-SHEET METHOD

The digestibility coefficients and biological values of proteins from red ants (*Ecophylla smaragdina*) have been studied at 10 to 15 per cent levels of intake. No appreciable difference could be found in the average figures obtained at the two levels of protein intake.

NUTRITION AND ITS BEARING ON PREVENTABLE BLINDNESS AND EYE DISEASES IN BENGAL

1. Conjunctival pigmentation, either alone or in combination with xerosis or Bitot's spots, is not necessarily a sign of vitamin-A deficiency.

2. Keratomalacia is most common in children below 5 years of age. About 10.5 per 10,000 of infants suffer from keratomalacia in Calcutta.

3. Vitamin A by parenteral administration is the quickest and most effective way of treating the disease. This method is especially indicated in cases associated with diarrhoea or jaundice.

Luffa acutangula: THE CHEMICAL AND PHARMACOLOGICAL INVESTIGATION OF *Luffa* SEEDS

1. The chemistry and pharmacology of the *luffa* seed have been studied.

2. It contains a fixed oil, a saponin and an enzyme.

3. It causes vomiting and purging in dogs. In small doses it causes nausea and salivation.

4. Its use in indigenous medicine as an expectorant and emetic has a rational basis. It is a very bitter substance and is worth a clinical trial in human beings.

THE PHARMACOLOGICAL ACTION ON THE CIRCULATORY SYSTEM OF A BITTER PRINCIPLE ISOLATED FROM *Securigera securidaca* (LINN.) DAGEN *et* DÖRFLER (N. O. LEGUMINOSÆ)

1. The bitter principle isolated from *Securigera securidaca* produces its pressor effect on circulation by its direct action on the cardiac musculature and plain muscle of the blood vessels and also partly by its action on the sympathetic nerve-endings.

2. The fall of blood pressure observed with bigger doses of the bitter principle is due to the stimulation of the vagal centre in the medulla.

HYPNOTIC EFFECT OF *Rauwolfia serpentina*: THE PRINCIPLE UNDERLYING THIS ACTION, ITS PROBABLE NATURE

1. The alkaloids *ajmaline*, *serpentine* and *serpentinine* of *Rauwolfia serpentina* are medullary stimulants and provoke convulsion and anoxæmia.

2. The sedative and hypnotic properties are present mainly in the alcoholic extract, and in the total alkaloids free from *ajmaline*, *serpentine* and *serpentinine*.

3. The hypnotic principle antagonizes the medullary stimulation of *picrotoxin* and has depressant action on the medullary centres.

STUDIES IN HÆMOLYSIS

The tables and graphs show very explicitly what occurs to the circulating red cells when a hæmolytic serum is given intravenously.

A massive hæmolysis occurs: this is followed by hæmoglobinæmia and hæmoglobinuria. The remaining blood cells are markedly spherocytic. These cells show increasing susceptibility to hypotonic saline solutions, but apparently not to any great extent to normal hæmolytic processes, since some of them survive for nearly three weeks (against the normal life of four weeks of the monkey's red cells).

As these cells disappear from the circulation they are replaced by larger cells which are not spherocytic and withstand hypotonic saline normally; these cells can be shown to be reticulocytes. The reticulocytes as they mature become reduced in diameter, so that

eventually the Price-Jones' curve is the same as before any hæmolytic serum was given.

After the action of the hæmolysin the mean corpuscular volume (MCV) of the red cells is also reduced. Thus, both the red cell diameters and volume are reduced; the explanation of this is not clear, and this point is discussed.

It would thus appear that though the life of the spherocyte may possibly be shorter than that of the normal cell, it cannot be considered that the assumption of the spherocytic shape is an *immediate* prelude to normal hæmolysis. It suggests rather that, though the assumption of the spherocytic shape may lead to intravascular disintegration of the red cell, if the effect falls short of this, it does not materially shorten the life of the red cell. A similar state of affairs exists in congenital hæmolytic icterus, where removal of the spleen stops the increased rate of destruction of red cells, but does not markedly affect the spherocytosis.

The observation indicates that the mechanism of *excess* hæmolysis resulting from injection of a hæmolytic serum may be similar to the mechanism of *excessive* blood destruction in congenital hæmolytic anæmia (and possibly to that in blackwater fever), but is quite different from that of physiological hæmolysis.

ON THE FRAGILITY OF ERYTHROCYTES. PART I

1. A preliminary investigation with an attempt to correlate the fragility and average diameter of the erythrocytes of several species of animals was carried out.

2. The fragility of erythrocytes belonging to certain species of animals was found to vary inversely as their average diameter.

SURFACE TENSION AND HÆMOLYSIS

1. Several well-known hæmolytic agents, such as saponin, sodium glycocholate, sodium taurocholate, sodium oleate, cyclamin and cobra venom, were studied with a view to find out if there were any correlation between the hæmolytic activity and the surface tension of the respective solutions.

2. With none of the hæmolysins examined was surface tension found to play any effective part in the initiation of the process of hæmolysis.

3. While, broadly speaking, the lowering of surface tension facilitates and its increase tends to retard hæmolysis, the part played by surface tension with respect to hæmolysis is only a secondary one and sometimes an increased surface tension may be attended with more rapid hæmolysis.

Intramuscular Pressure

The Physiology of the Venopressor Mechanism and the Importance of Maintaining Intramuscular Pressure in the Treatment of the Peripheral Collapse of Shock and Shock-Like States

By L. GUNTHER

(Abstracted from the *United States Naval Medical Bulletin*, Vol. 41, March 1943, p. 414)

THE intravenous use of coramine in adequate doses from 5 to 10 c.c. is a valuable adjunct in the treatment of the immediate period of shock. The clinical evidence of peripheral collapse rapidly regresses for a period of an hour or more. The effect can be repeated by a second intravenous administration. The time interval is important. Peripheral circulatory support is obtained during the immediate period when fatalities occur. Its use should permit survival until such time when serum and other useful therapeutic procedures can be instituted.

The Prevention of Renal Obstruction during Sulphadiazine Therapy

By C. L. FOX, Jr., M.D.
OLE J. JENSEN, Jr., M.D.

and

LIEUT. G. H. MUDGE

(Abstracted from the *Journal of the American Medical Association*, Vol. 121, 3rd April, 1943, p. 1147)

1. THERE is great variation in the urinary solubility of sulphadiazine, sulphathiazole and their acetyl forms over the physiologic pH range.

2. Since the solubility of these drugs is greatly increased in alkaline urine, maintenance of a consistently alkaline urine was tried as a means of preventing renal obstruction during sulphadiazine therapy.

3. Two patients with subacute bacterial endocarditis were given massive doses of sulphadiazine, and with certain exceptions their urine was maintained

consistently alkaline with large doses of bicarbonate (10 to 20 gm. daily). No alkalosis or oedema resulted.

4. High concentrations of sulphadiazine were held in solution in alkaline urine; oliguria and renal obstruction were prevented. Crystalluria occurred in those urine specimens in which the pH fell below the *in vitro* solubility limits.

5. The quantity of bicarbonate to be given should be judged by the pH of the urine. To maintain sulphadiazine in solution during full therapeutic doses, a pH of 7.5 or higher is essential.

6. When alkaline urine is voided with high concentrations of sulphadiazine in solution decreasing the pH slightly will immediately precipitate the drug.

7. In the renal (pelves and ureters) lavage therapy of renal obstruction caused by one of the sulphonamide compounds, alkaline bicarbonate or carbonate solutions are recommended, since these will dissolve drug crystals much better than warm water or isotonic solution of sodium chloride. Utilization of this information in routine therapy with sulphathiazole and sulphadiazine in average doses would remove the hazard of their renal complications.

Reviews

HANDBOOK OF PHYSIOLOGY AND BIOCHEMISTRY.

—By The Late W. D. Halliburton, M.D., LL.D., F.R.C.P., F.R.S., and R. J. S. McDowall, M.D., D.Sc., F.R.C.P. (Edin.). Thirty-seventh Edition, 1942. John Murray, London. Pp. x plus 977. Illustrated. Price, 21s.

New editions of this familiar handbook have appeared regularly and at frequent intervals; this keeps it up to date and at the same time reflects its popularity. In the present edition considerable changes have been made, particularly in regard to the hormones, sensation, blood and physical chemistry. The recently added features, the insertion in dark type of points of special emphasis, of figures to be memorized and of pages for notes at the end of chapters have been retained.

The book has become a stand-by of medical students for many years, and we have no doubt that it will continue to serve the useful purpose.

R. N. C.

NEW ASPECTS OF CHEAP FOOD.—By Rudolph Keller (Prague), D.Sc., B.Sc. 1943. Research Books Limited in Association with William Heinemann (Medical Books), Limited (99, Great Russell Street, W.C.1), London. Price, 1s. 6d.

THIS little book surveys the scientific and economic aspects of nutrition as they confront Great Britain to-day. The author points out that a cheap and nourishing diet may be a decisive weapon in war time, and that the lack of food policy has led that country into the present situation involving as it does the use of much valuable shipping space for bringing supplies from overseas. Years before the war Japan and Germany, with the co-operation of scientists and economists, worked hard to make foods which are cheap and efficient and made considerable progress in this respect. The Germans boasted that they achieved their great victories in the West by the efficient feeding of their motorized divisions with soya bean preparations. The author advises that the British should adopt this article as a part substitute for meat; it is rich in protein and fat, and cooked with vegetables, potatoes, etc., can be made into a very tasty dish. The neglect of this important food, he quotes from the *Times*, is one of the greatest errors of British food politics. While the Japanese could get it for a penny, the British had to pay nearly a shilling for a pound. He has much to say about the 'weak point in English cooking' of vegetables and potatoes and suggests several methods to improve their taste and nutritive value. Among his other

recommendations are eating part of the vegetables raw as salads, low salt diet and use of cane molasses not only for cheapness but for its dietary value. Many of the author's ideas are good but are presented in a somewhat disjointed manner.

R. N. C.

THE EXAMINATION OF WATERS AND WATER SUPPLIES.—By Ernest Victor Suckling, M.B., B.S. (Lond.), M.R.C.S., L.R.C.P., D.P.H. Fifth Edition, 1943. J. and A. Churchill Limited, London. Pp. x plus 849, with 63 illustrations. Price, £3-0-0

UNLIKE most other books on this subject, Dr. Suckling's fifth edition is not a mere manual for laboratory practice, but deals in a comprehensive manner with the various aspects of water relating to geology, for industrial and domestic purposes, relation to various diseases and the necessary treatments for industrial water and potable supplies.

The book is divided into eight parts. The first two parts relate to geological aspects of water supplies and are similar to the older editions. The next two parts deal with quality of water and interpretation of water analysis. The conclusions of these sections are based on actual practical experience and not merely on theory. The paragraphs on electrical conductivity are especially interesting and should be studied carefully by workers in the United States who have neglected to a great degree the usefulness of electrical conductivity in routine analysis.

The bacteriological section has been considerably rewritten and contains excellent chapters on water bacteriology, specially that part relating to sulphur bacteria.

The chemical sections review established analytical methods and also take up the recent findings for the detection and estimation of fluorine.

Chlorination, specially breakpoint chlorination developed in America, is taken up in detail, and it is noted with satisfaction that the contact period in simple chlorination is recommended to be not less than $\frac{1}{2}$ hour which is similar to the reviewer's experience of six years' research on tropical waters in India.

The eighth and last section dealing with purification and treatment of water is somewhat limited from the theoretical point of view, but this does not detract from the value of the book.

This book is a valuable reference for all workers, engineers, chemists, and medical men, but it is specially

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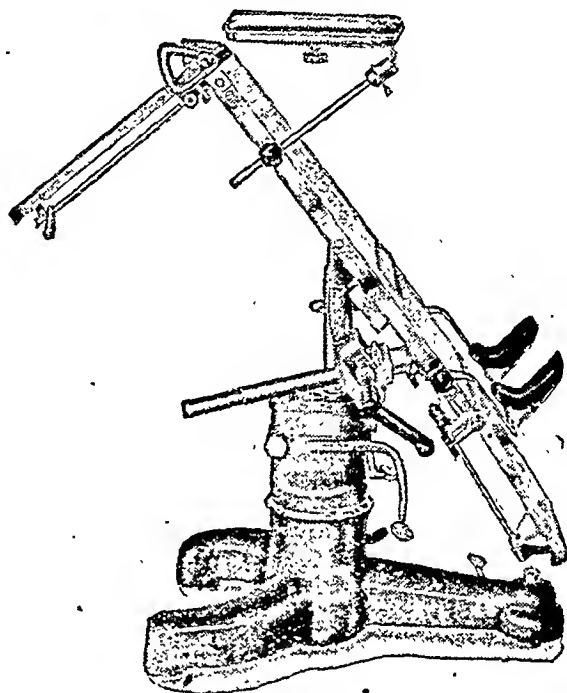
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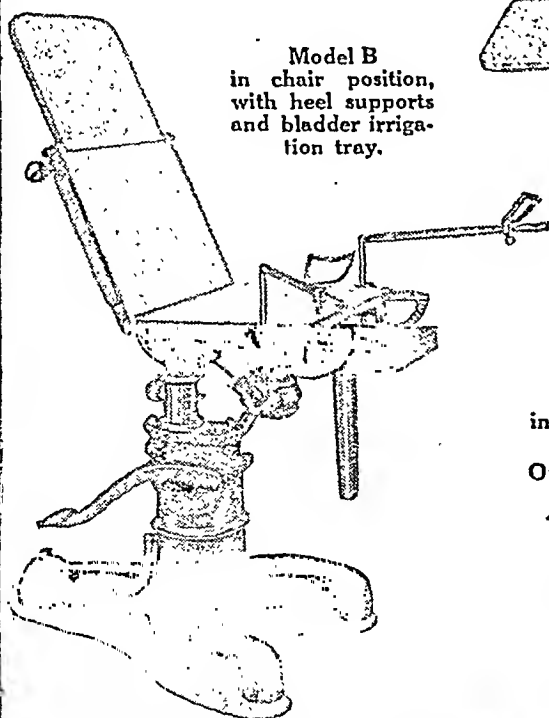
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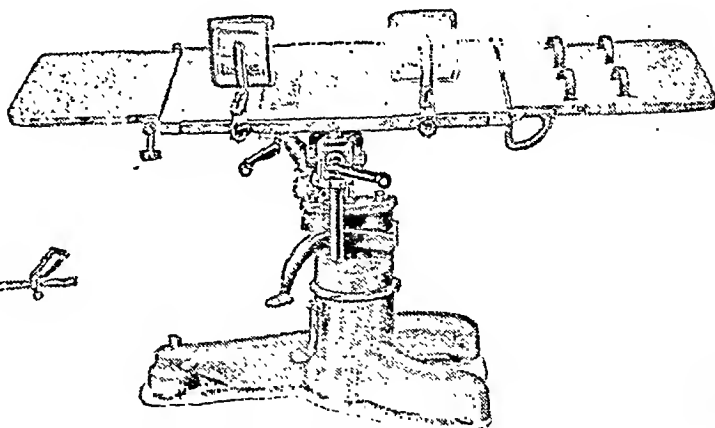


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recommended as a text for graduate students who are specializing in Public Health Engineering.

B. R. D.

PSYCHOLOGICAL MEDICINE: A SHORT INTRODUCTION TO PSYCHIATRY. WITH AN APPENDIX ON WAR-TIME PSYCHIATRY.—By Desmond Curran, M.B., F.R.C.P., D.P.M., and Eric Guttman, M.D., L.R.C.P. (Edin.). 1943. E. & S. Livingstone, Edinburgh. Pp. viii plus 188. Illustrated. Price, 10s. 6d.; postage, 6d.

THIS small and handy volume of 182 pages consists of two parts. The first is a very elementary description of psychiatric disorders with very little emphasis on psychotherapy, psychological mechanisms or theory. It rightly stresses the need for a fuller study of the patient's underlying personality. Actually it is a revised edition of the section on psychological medicine by the same authors in J. J. Conybeare's Textbook of Medicine long passages of which have simply been reprinted. It thus fulfils the same purpose as the section in this textbook, namely, an elementary introduction for medical students, and would be of no use to those already in possession of the above textbook or to the specialist. The section on war time psychiatry is practical and should be useful to medical officers who will also appreciate the fact that the volume is easy to carry about. It tends to over-simplify the nature of war time neuroses. Although many cases, it is true, can be cured by relatively superficial psychotherapy or environmental adjustment, others will require consideration of more deep-rooted conflicts, which the present volume tends to under-estimate. The best part of the book is the section on head injuries which is up to date, thorough and of interest even to the specialist. The book is well illustrated. It will be useful to medical students or practitioners not in possession of a similar section in one of their general medical textbooks, and to the medical officers in the services as an elementary introduction into psychiatric diagnosis.

M. T.

TRAINING FOR CHILDBIRTH: FROM THE MOTHER'S POINT OF VIEW.—By M. Randell, S.R.N., S.C.M., T.M.M.G. Third Edition. 1943. J. and A. Churchill Limited, London. Pp. viii plus 123, with 128 illustrations. Price, 10s. 6d.

THE core of Miss Randell's text lies in the description of mind and muscle training which she advocates to ensure a comfortable pregnancy and an easy labour, and to limit to the minimum the toll taken by childbirth upon the physical and mental equilibrium of the mother.

The system covers the principles and methods of achieving mental and physical relaxation, exercises and postures for the pre-natal period, postures to be adopted more particularly during the first stage of labour, and a group of post-natal exercises. This section is freely illustrated by photographs, diagrams and small-figure drawings, and an interesting feature is the addition of extracts from the diaries of first labours made by some of the author's patients.

Probably the exigencies of war time printing are responsible for the arrangement of the illustrations, of the exercises, as it seems possible that by classification and sectional illustration they might have been more advantageously and more simply demonstrated. The exercises seem almost unduly numerous, presented as they are. The post-natal exercises are perhaps those best presented. One wonders if the chapter on post-puerperal disabilities might not have been better placed earlier in the text as an introduction to the exercises. The author has quoted frequently from Dr. Kathleen Vaughan's book 'Safe Childbirth' and those who accept Dr. Vaughan's views will welcome this book as offering their practical application. It is difficult to evaluate in practical terms a book on this subject written for the well-educated woman and her obstetrician or maternity nurse, against the present lack of facilities for the study and organization of physiotherapy in India.

Unless schools of massage and physiotherapy are established and take the lead in providing trained personnel as well as offering organized demonstration of the value of posture and exercises upon labour and the puerperium, it is hard to suggest that there will be a ready demand in this country for a book of this type. This is a subject where example outweighs precept in stimulating interest.

L. G.

MEDICAL RESEARCH COUNCIL. SPECIAL REPORT SERIES, NO. 247. THE EPIDEMIOLOGY OF DIPHTHERIA DURING THE LAST FORTY YEARS.—By W. T. Russell. 1943. Published by His Majesty's Stationery Office, London. Pp. 58. Illustrated. Price, 1s.

THIS report deals statistically with the incidence and mortality of diphtheria in Britain during the last forty years, and includes a study of the results of protective inoculation of children, with particular reference to experience in the United States and Canada, where inoculation has been extensively practised. There is very strong evidence that immunization has reduced the morbidity and mortality from diphtheria in New York City and in Toronto. The number of children immunized in Britain before 1940 was very small but since then fairly satisfactory progress has been made. The conclusions to be drawn from the evidence presented are in favour of active immunization against this disease as a life-saving measure.

R. N. C.

Abstracts from Reports

ANNUAL REPORT ON THE HEALTH OF THE ARMY IN INDIA FOR THE YEAR 1941. VOLUME IV. PART I

'THE health of the army for 1941, while not so good as in former years, is considered to have been on the whole fairly satisfactory, taking into account the many adverse factors present throughout the year.' Thus comments Major-General A. Campbell-Munro, D.M.S. in India. For both British and Indian other ranks, admissions to hospital rose considerably above those of the years immediately preceding 1941. Factors which probably affected the incidence of disease were the inexperience of young medical officers, alteration in age composition of the army and decline in the standard of physical fitness, harder work, civilian soldiers and marked increase in the movements of units, often through malarious areas. In addition to these factors, some overcrowding and lack of sufficient warm clothing had an effect in the case of Indian troops.

Malaria was the most prevailing disease. There was regression in the downward trend in its incidence, which had been apparent during recent years, the main reason being war conditions which necessitated change of anti-malaria personnel, location of troops in malarious areas, movements and operations in the malaria season, etc. *Sandfly fever* which had markedly decreased during the previous four years owing to intensive anti-sandfly campaign, chiefly by spraying, suddenly increased during the year owing to various causes. It is very satisfactory that the admission rate for *fevers of the enteric group* has been maintained at a low level as in the previous years; this is attributed almost entirely to efficient protection with TAB vaccine. The continued low rate is all the more noteworthy as diagnosis nowadays is much more accurate and in old days many cases would have been missed. On the other hand, the *dysentery-diarrhoea* group of diseases had a very high rate of incidence. There had been no tendency for this group to decrease during the last decade, but 1941 was the worst year. Various causes are mentioned in the report. 'Diarrhoea and mild dysentery are so common in new arrivals in India (Europeans) that they may be regarded as normal factors in acclimatization.' It is interesting to

note the percentage of cases of different types of dysentery that occurred in the army :—

	British	Indian
Dysentery, protozoal ..	10.81	5.43
" bacillary (proved) ..	49.69	44.56
" " (exudate) ..	10.74	14.42
" " (clinical) ..	28.76	35.59

Cholera was not common, there being only 25 cases among the British and 61 among the Indians, in the former case the cause was probably the table-boys and cooks, some of whom were found to be carriers of *V. cholerae*. Venereal diseases continued to increase as is the common experience in wartime. *Cerebro-spinal fever* also increased among Indian troops. Over-crowding which was prevalent no doubt contributed to it.

In 1941, a new anti-malaria organization was drawn up consisting of an adviser in Malariology and 20 civilian medical graduates and 60 civilian science graduates to be posted at selected stations as anti-malaria medical officers and assistants respectively. The recurring cost of the scheme will be over 10 lacs.

Correspondence

A PLEA FOR MEDICAL HISTORY EXHIBITIONS IN INDIA

SIR,—Medical men who have attended the meetings of the British Medical Association or even read the proceedings of the above meetings in Oxford, Cambridge, London or Australia may remember how interesting and instructive medical history exhibitions can be.

As early as in 1936, I published a plea in the *British Medical Journal* that the rare and instructive Indian medical manuscripts in Oxford, Cambridge and London may also be exhibited along with the British, European and Arabian exhibits at the time of the meetings of the British Medical Association. Professor Charles Singer of London who communicated my letter to the *British Medical Journal* stated that he and the Editor fully endorsed my plea.

I have also made a plea for similar medical history exhibitions in India in a paper read before the medical section of the Science Congress held at Calcutta in January 1938. The same paper, 'A plea for the promotion for the study of history of medicine' has been printed in the *Journal of Indian Medical Association*, September issue, 1938.

At the Madras session of the Science Congress in 1940 in my paper 'The present position of the history of medicine in India' (published in *Journal of Indian Medical Association*, May 1940) I made the following appeal. 'Another matter which has been sadly neglected and which deserves the attention of all organizers of conferences and congresses is the value and inspiration of an exhibition of old books, manuscripts and printed ones, illustrating the progress of medicine in space and time. . . . Indian cities where medical conferences are held are rich in materials for such exhibition and with the co-operation of the university library, oriental libraries or private learned bodies, it should not be difficult to organize a fairly representative exhibition of rare and old manuscripts of early printed editions, of portraits and paintings pertaining to medicine and of medical relics and curiosities.' In the ensuing discussion, some leading members of the medical section and professors of the medical colleges at Madras asked me if I could not arrange for such an exhibition for the next day. I pointed out that I would be able to do so if the local secretaries of the Reception Committee could persuade the authorities of the medical college library and the university library and the

oriental library to lend certain of the exhibits, according to the list I prepare. Ultimately, the whole thing fizzled out, as the time at our disposal was considered too short.

Now that the Indian Science Congress is holding its session in a state famous for the promotion of oriental studies and publications, as well as for the collection of art treasures and archaeological relics, I would appeal, in my individual capacity as a student of history of medicine, and in a representative capacity, as the corresponding member of the American Association of the History of Medicine, to the organizers and Reception Committee of the Science Congress in Trivandrum to take the initiative and have, side by side with the usual industrial or commercial or scientific exhibition, a cultural and medico-historical exhibition of the type till now arranged only in America and Europe.

MEDICAL HISTORY EXHIBITION

List of exhibits to be collected and included :—

I. GODS OF HEALING

(a) Idols, (b) dolls, (c) plaques, (d) stone panels, (e) images, (f) pen and ink sketches, (g) paintings on paper or glass, (h) reproduction of wall paintings, (i) photos of temples or of idols of gods worshipped in the State for special diseases, (j) votive offerings.

II. MEDICINE IN ART

Stones, sculptures or panels or paintings or outline drawings illustrating incidents from Indian legends or epics showing the wounded or the sick or treatment of the sick.

III. MEDICAL MANUSCRIPTS

(a) Ancient and medieval Sanskrit medical classics, (b) manuscripts in South Indian languages, (c) manuscripts in European languages (Portuguese or English records dealing with medicines or diseases or physicians).

IV. EARLY PRINTED BOOKS IN MEDICINE

(a) Books in European languages (Portuguese and English, etc.), (b) books in South Indian languages, (c) books in Sanskrit.

V. RELICS OF MEDICAL INTEREST

(a) Flints, bones, knives, lancets, forceps, splints, (b) containers of medicine, mortars, etc.

VI. RECORDS OF HEREDITARY PHYSICIANS

(a) Family genealogy with sketches or notes on physicians and notebooks on medicine kept by families, (b) records of seventeenth and eighteenth century missionaries dealing with medical relief, (c) records, sketches and descriptions of the early Portuguese, English or other hospitals in the State and surrounding areas.

VII. DESCRIPTION OF EPIDEMICS OR SPECIAL DISEASES FROM STATE RECORDS OR PRIVATE RECORDS

VIII. MEDICAL LORE IN LITERATURE

(a) Any Malayalam classics, describing doctors on their work, with a short abstract in English, (b) books dealing with merits and virtues of sacred places and mineral springs.

IX. MEDICINE IN FOLK-LORE

(a) Sayings or songs, (b) amulets and charms.

X. BOOKS ON THE HISTORY OF MEDICINE

(a) Books dealing with history of medicine in general, (b) books dealing with special branches of medicines, (c) books dealing with history of medicine in India, (d) what other countries are doing for the promotion of the studies in history of medicine.

D. V. SUBBA REDDY, M.B., B.S.,
Andhra Medical College, Vizagapatam.
Correspondence Member, American
Association of History of Medicine.

12th September, 1943.

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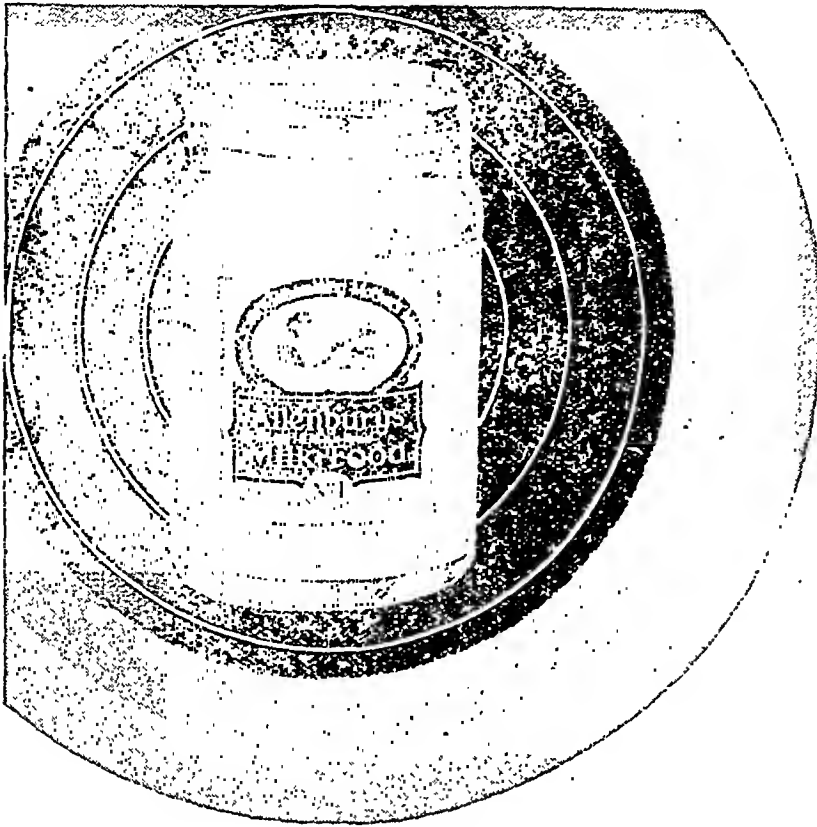
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THE TREATMENT OF SHOCK

SIR,—The time is ripe when a fundamental change in the treatment of shock is indicated and I wish to draw the attention of the various medical and nursing bodies to the radical change in the concept of shock and its treatment that has been evolved since the commencement of this war, as summarized, for instance, in editorials in the *Journal of the American Medical Association*, 1943, **121**, p. 432 and p. 1352.

It may be pointed out that the customary treatment with blankets and hot water bottles in case of shock has never been based on experimental findings, but rather on tradition. The modern view defines shock as the manifestation of circulatory collapse and the peripheral fall in temperature (cold clammy skin), due to the failure of capillary circulation, is not necessarily accompanied by a corresponding fall in body (rectal) temperature. The anoxia (lack of oxygen in the system) caused thereby is only aggravated by the application of heat. The life of the tissues may be considerably shortened by such treatment and the chances of the recovery of the patient correspondingly reduced.

Experiments on rats, dogs, rabbits and guinea-pigs, in which shock was produced by exposure of the abdominal viscera and intestinal stripping, resulted in disclosing the optimal survival temperature for the first named at about 77°F. and for the others at body temperature (Wakim and Gatch, *J. Amer. Med. Assoc.*, 1943, **121**, 903).

Other experiments on rats suffering from shock caused by extensive superficial burns have shown that the best survival temperature is 75°F. and raising or lowering the temperature either 20°F. above or below the optimum reduced the chances of recovery by 100 per cent (Elman and co-workers, *Proc. Soc. Exp. Biol. and Med.*, 1942, **51**, 350).

In this connection it would be well to recall the introduction of refrigeration anaesthesia in major amputations and in trauma of the limbs, in the control of hæmorrhage, pain, progressive shock and infection during transportation (*J. Amer. Med. Assoc.*, 1943, **122**, 177; *Brit. Med. J.*, 1943, *i*, 573).

Finally, direct field observations in the Spanish Civil War and in the Libyan campaign of the present world war have demonstrated the proneness of even light casualties to go into shock in the summer heat, much severer cases, on the other hand, remaining conscious in cooler weather.

The logical treatment of shock, therefore, in accordance with our present knowledge, based on animal experiments, as well as on observations on war casualties, is to keep the patient comfortably cool, to refrain from applying external heat unless the rectal temperature has fallen below 96°F. and in all cases where the patient is conscious, to follow his or her own wishes regarding the application of warmth or the removal of clothing.

AMIN TYABJI.

CHEMICAL, INDUSTRIAL AND
PHARMACEUTICAL LABORATORIES,
LIMITED, 289, BELLASIS ROAD,
BYCULLA, BOMBAY,
2nd October, 1943.

THE USE AND ABUSE OF LIQUID PARAFFIN

SIR,—While reading the article on 'The Use and Abuse of Liquid Paraffin' by L. K. Upamanyu in No. 9, 1943, of the *Indian Medical Gazette* I was reminded of another injurious effect of liquid paraffin which might be of interest to your readers. Since 1925 communications appeared on pulmonary aspirations of oily substances eventually recognized as a clinical entity under the name of 'Lipoid Pneumonia', sometimes mentioned also as oil pneumonia, aspirational pneumonia and pneumolipoidosis. Up to 1940, 136 cases have been reported. Since then I am aware only of five further communications (see below). Although the number of reported observations seems

small compared with the tremendous amount of mineral oil used throughout the world, the correct diagnosis is very likely to remain unrecognized in the majority of occurrences. X-ray examination, in many instances, does not reveal any pathognomonic feature, particularly in children. Positive x-ray findings frequently suggest various issues such as fibrosis, bronchiectasis, malignant growths, tuberculosis, etc. The clinical aspect accordingly is just as puzzling. Aspiration biopsy, as mentioned by Farber *et al.* (1942), provided the pleural space is obliterated, remains an undertaking suitable only for hospitals. Careful history taking will often lead into the right direction.

In 1940, the *Journal of the American Medical Association*, in an editorial, drew particular attention to the dangers of promiscuous use of nasal oil sprays and the internal administration of various oils. It is generally held that the use of oily nasal drops, cod-liver oil, liquid paraffin, etc., is injudicious in small or weak children as well as in debilitated conditions of adults and old age, summarily in all cases where difficulty in breathing and swallowing might provide the necessary mechanism for aspiration.

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7, 334.

K. EISENSTAEDT, M.D.

SUSSEX LODGE,
JAMNAGAR (KATHIAWAR),
10th October, 1943.

QUININE SULPHATE FOR INTRAMUSCULAR INJECTIONS

SIR,—Owing to the shortage of quinine by-hydrochloride may we draw attention to the following method of using quinine sulphate for intramuscular injections which we have found to be successful in malaria? About 6,000 injections have been given in the past 12 months without any abscess formation and the therapeutic results have been as satisfactory as quinine bi-hydrochloride. Even infants, a month old, have been given the injection.

The usual dose for adults is 10 grains, given in the buttocks, though we have used as much as 15 grains in some cases. We have found no difference as regards local tenderness after the injection between quinine sulphate and quinine by-hydrochloride. Our technique of preparation is as follows:—

(i) Add 100 minims of dilute hydrochloric acid (B.P.) to 10 c.cm. of distilled water and then dissolve 100 grains of quinine sulphate powder in the above. Now add enough distilled water to make the total quantity 20 c.cm. Each 1 c.cm. now contains 5 grains of quinine sulphate in solution.

(ii) Filter solution through filter paper. To prevent the solution being absorbed into the filter paper, first moisten the paper with distilled water.

(iii) After filtering boil the solution and keep in a sterile stoppered bottle. It is now ready for use. If the solution is not used the same day then the required quantity to be used can be boiled again. The therapeutic efficacy of the quinine is not affected, in our experience, by double boiling.

(iv) Use only dilute hydrochloric acid and not dilute sulphuric acid for dissolving the quinine sulphate, as

with the latter the quinine crystallizes to the bottom after a short while.

CHRISTIE MCGUIRE,
Medical Officer,
M. L. CHAKRAVARTY,
Assistant Medical Officer,
and
G. C. KARMAKAR,
Assistant Medical Officer.

NEWLANDS T.E. AND P.O.
DOOARS,
5th September, 1943.

ROYAL COLLEGE OF SURGEONS OF ENGLAND

SIR,—I have pleasure in sending you a copy of a notice concerning the revision of the regulations for the Fellowship of the Royal College of Surgeons of England, with a copy of the new regulations.

As the changes embodied in these regulations are possibly the most important that have been made since the Fellowship was instituted under the Charter of 1843, it is hoped that you may be good enough to find

space for a special Editorial note on the subject. A point, in this connection, which will doubtless not escape your notice is the rearrangement of the dates of the examination, enabling those who are eligible and may wish to do so, to enter for both the Primary and the Final at the same time (*vide* Regn. 10)—and this may be of special convenience to candidates from overseas.

HORACE H. REW,
Director of Examinations,
Royal College of Surgeons
of England.

EXAMINATION HALL,
8-11, QUEEN SQUARE,
LONDON, W.C.1.
7th July, 1943.

[Note.—We have received the above letter from the Director of Examinations, Royal College of Surgeons of England, enclosing a circular concerning the revision of the regulations for F.R.C.S. which is in the *Medical News Section* of this number (see p. 605).—EDITOR, J. M. G.]

Service Notes

APPOINTMENTS AND TRANSFERS

On vacating the post of Officer on Special Duty in the Medical Division of the Directorate General of Supply, the services of Colonel (Local Brigadier) G. Covell, C.I.E., V.H.S., were replaced at the disposal of the Education, Health and Lands Department, with effect from the 21st September, 1943.

Colonel J. B. Hance, C.I.E., O.B.E., V.H.S., Deputy Director-General, Indian Medical Service, was appointed Director-General, Indian Medical Service, with effect from the 4th October, 1943.

Lieutenant-Colonel H. W. Mulligan is appointed Assistant Director, Central Research Institute, Kasauli, with effect from the forenoon of the 15th August, 1943.

Major Jaswant Singh, Assistant Director, Malaria Institute of India, was appointed to officiate as Director of the Institution in addition to his own duties during the absence on deputation of Colonel (Local Brigadier) G. Covell, C.I.E., V.H.S.

Major W. Scott, Civil Surgeon, Amraoti, returned from leave and resumed charge of the office of the Civil Surgeon, Amraoti, on the forenoon of 17th September, 1943.

LAND FORCES

INDIAN MEDICAL SERVICE—SECONDED TO INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

To be Captains

Alan Rex Adderley. Dated 21st February, 1943.
Mohammed Yousuff Siddiqi. Dated 4th April, 1943.

7th August, 1943

Rabindra Nath Chatterjee. Murari Mohon Som.

11th August, 1943

Sachindra Nath Roy. Suprabhat Mukherjee.

14th August, 1943

Esmail Jafferbhaji Javeri. Debabrata Ray Mahasaya.
Jagan Nath Jaswal. Dated 1st September, 1943.
Rabindra Nath Mittal. Dated 11th September, 1943.
Indra Nath Sarkar. Dated 13th September, 1943.

14th September, 1943

Sitaramaswami Batreddi. Krishna Rao Bogolu.
Rajuvadan Elliah. Rani Prasad Agrawal.
Sukumar Sanjay. Manindra Kumar De.
Narendra Nath Roy. Dated 15th September, 1943.
Edward Gordon Pyne. Dated 15th June, 1943.

To be Major

Ramesh Chandra Basu. Dated 7th July, 1943.

To be Captains

Narayan Vaman Khalap. Dated 4th June, 1943.

16th June, 1943

Malik Shaikat Hasan. Chaudhry, Abdul Majid.
Daryao Singh.

7th July, 1943

Sibdas Hazra. Hirandra Lal Bannerji.
Radha Ranjan Chaudhuri. Jagannath Maitra.
Gouri Charan Dutt. Harendra Bahadur Sinha.
Frank Patrick Mascarenhas. Dated 8th July, 1943.
Balai Lal Chuckerbutty. Dated 5th August, 1943.

6th August, 1943

Sudhmay Bhattacharyya. Digumarthi Sundarasiva-
Indu Bhushan Ghosh. rao.

7th August, 1943

Manoranjan Ray. Amarendra Sen Gupta.
Randhir Singh. Dated 8th August, 1943.
Swaroop Nath Wanchoo. Dated 14th August, 1943.
Sukomal Sen. Dated 7th July, 1943.
Krishna Kali Bose. Dated 6th August, 1943.
Arun Kumar Lahiri. Dated 7th August, 1943.
Krishnaswamy Venkataraman. Dated 13th August, 1943.

14th August, 1943

Khagendra Nath Sen Gupta.
Taraprasad Bhadury.
Sreevasthav Kayasth Sudarsan Lal.
Mohammad Afimuddin.
Murthappa Shamurao Narasimha Murthy. Dated 7th August, 1943.
Onkar Swaroop Dewan. Dated 8th August, 1943.
Trimbak Balwant Sonwancy. Dated 13th August, 1943.
Akkanaipragada Rama Mohan Rau. Dated 14th September, 1943.
N. E. Bennett. Dated 8th August, 1943.
Mohomed Zainulabedeem. Dated 14th September, 1943.
Mohammad Khalil-ur-Rahman Siddiqui. Dated 15th September, 1943.

To be Lieutenants

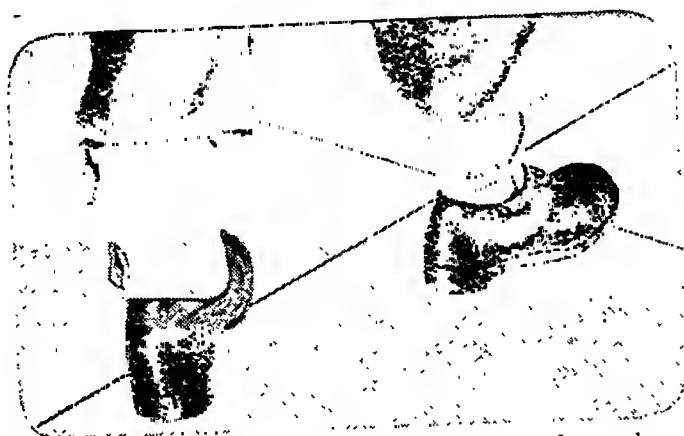
Brij Nath Bhargava. Dated 9th January, 1943.

16th June, 1943

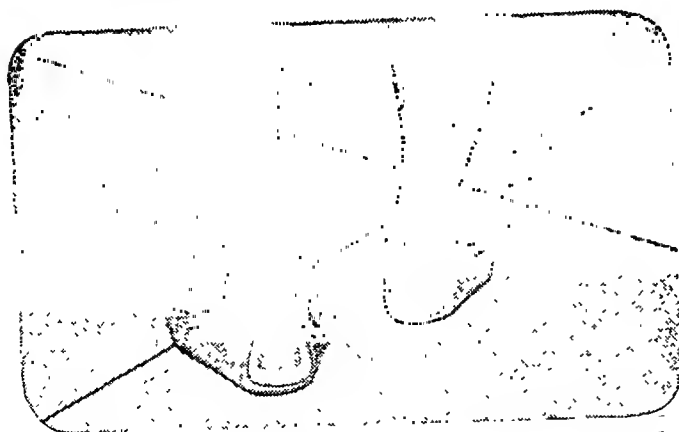
Inayat Ullah Chowdry. Dev Raj Aggarwal.
Maxwell Joseph Van Ross. Dated 24th June, 1943.
Eardley George Clarkson. Dated 2nd July, 1943.

E.D.6.

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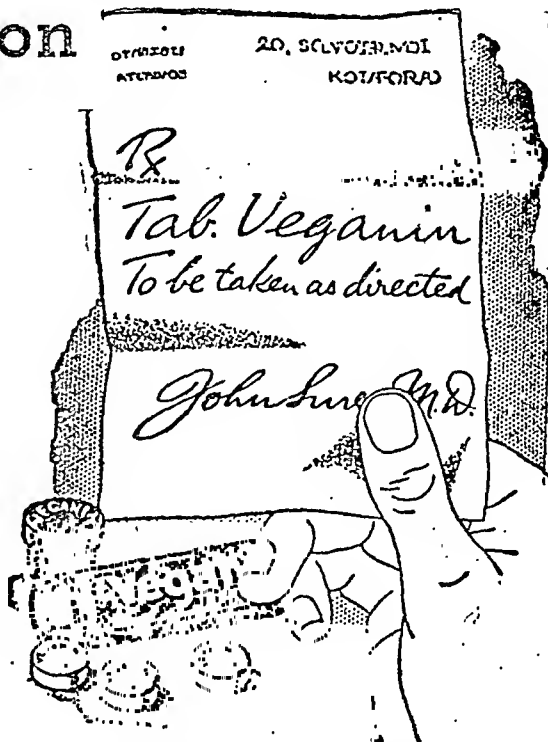
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7th July, 1943

Areth Kochugovindan. Sadasivam Subramaniam.
 Amaresh Chandra Bose. Kadaba Parthasarathy.
 Autar Singh Bhasin. Madireddi Gevenda Rao.
 Kumarish Chandra Banerjee.

Pandit Ramanjulu Naidu. Dated 8th July, 1943.

6th August, 1943.

Gerald Maxwell Muller. Davendra Nath Gupta.

7th August, 1943

Balraj Bhatia. Mohammad Farhat Hussain Malik.

Stephen Francis D'Costa. Dated 12th August, 1943.

Autar Krishan Choudhary. Dated 16th June, 1943.

13th September, 1943

Rabindra Nath Sil. Amulya Nath Datta.
 Azizur Rahman Chowdhury.

7th July, 1943

Shiv Nath Kapur. Kidar Nath Sharma.
 Siri Krishan Chopra. Dated 7th August, 1943.

13th August, 1943

Prafulla Chandra Lala. Shamim Aon Jafarey.
 Mohammad Latif.

Bhagwan Das Kumar. Dated 7th August, 1943.

Duncan Anthony Leonard Gibson. Dated 12th August, 1943.

Joseph Michael Francis D'Mello. Dated 22nd August, 1943.

Ernest John Goodsir Cullen. Dated 22nd August, 1943.

14th September, 1943

Onkar Nath Tyagi. Aboni Bhattacharya.
 Mahadeo Keshav Bodas. Hrishikesh Dutt.
 Golok Chand Dey.

To be Lieutenant

Samuel McClatchie. Dated 23rd January, 1942.

To be Lieutenants (on probation)

17th May, 1943

Gertrude Olga Walker Millington.
 Clare Mary Rogan.

22nd February, 1943

Beryl Alberta Barlow. Lillian Margaret Reeve.
 Lorna Christine Petersen. Dated 13th April, 1943.

(WITHIN INDIAN LIMITS)

To be Captains

Suresh Bhattacharyya. Dated 12th July, 1943.

Loyola Aivaro Francisco Jose Ignacio Furtado. Dated 7th August, 1943.

Santibrata Ghosh. Dated 13th September, 1943.

Chanasvram Das. Dated 7th July, 1943.

Bhagat Singh. Dated 7th August, 1943.

To be Lieutenant

Vittal Raghavendra Rao. Dated 8th July, 1943.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
 (Emergency Commissions)

To be Captain for service with Indian Air Force

Ambil Tirumala Swamy Srinivasa Iyengar. Dated 14th July, 1943.

The undermentioned officers of the I.M.S. (E.C.) revert from I.A.M.C. and are seconded for service with the Indian Air Force :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
 (Emergency Commissions)

7th July, 1943

Lieutenant J. H. F. Manekshaw.
 Lieutenant M. R. Mahmood.
 Lieutenant G. N. Sen Gupta.
 Lieutenant A. M. Sharangapani. Dated 2nd August, 1943.

Lieutenant K. Kurian. Dated 7th August, 1943.

Lieutenant M. Hussain. Dated 9th August, 1943.

Lieutenant S. A. Hasnain. Dated 10th August, 1943.

The undermentioned officer of the I.M.S. (E.C.) reverts from I.A.M.C. and is seconded for service with the Royal Indian Navy :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE
 (Emergency Commissions)

Captain H. B. Sinha. Dated 8th September, 1943.
 (WOMEN'S BRANCH)

To be Captains

(Miss) Khorshed Irani. Dated 20th May, 1943.

(Mrs.) Amy Winifred Burrowes. Dated 6th August, 1943.

Miss Amy Jungalwalla. Dated 2nd August, 1943.

Mrs. May Frances Hutton. Dated 19th July, 1943.

9th August, 1943

Miss Dina Byramji Langrana.

Miss Dina Burjorji Lovji.

(Miss) Arne Rocha. Dated 12th August, 1943.

Miss Mary Hilda Juliet James. Dated 1st September, 1943.

To be Lieutenants

Miss Niamto Devi Chadda. Dated 20th September, 1943.

Miss Narasappa Manohara Bai. Dated 8th September, 1943.

Miss Perin Homi Baria. Dated 20th August, 1943.

INDIAN LAND FORCES

INDIAN MEDICAL SERVICE—SECONDED TO INDIAN ARMY
 MEDICAL CORPS
 (Emergency Commissions)

The undermentioned officers are transferred to the General Service Cadre, with effect from the dates specified :—

Captain L. S. Doraswamy. Dated 23rd August, 1943.

Captain W. D. Pande. Dated 3rd September, 1943.

Captain Kartar Singh Kalra. Dated 25th August, 1943.

Captain Suresh Bhattacharya. Dated 4th October, 1943.

LEAVE

Lieutenant-General Sir Gordon Jolly, K.C.I.E., K.H.F., Director-General, Indian Medical Service, was granted, preparatory to retirement, leave on average pay for 4 months and 19 days, with effect from the afternoon of the 3rd October, 1943.

PROMOTIONS

Colonel to be Major-General

J. B. Hance, C.I.E., O.B.E., V.H.S. Dated 8th November, 1943.

Lieutenant-Colonel to be Colonel

M. S. Joshi. Dated 7th July, 1943.

INDIAN MEDICAL SERVICE—SECONDED TO INDIAN ARMY
 MEDICAL CORPS

Lieutenant-Colonels to be Colonels

J. L. D. Yule. Dated 28th March, 1943.

V. N. Agate. Dated 16th May, 1943.

A. H. Harty, C.I.E. Dated 9th August, 1943.

Majors to be Lieutenant-Colonels

J. C. Drummond. Dated 22nd August, 1943.

D. MacD. Fraser. Dated 25th August, 1943.

J. F. Shepherd. Dated 29th August, 1943.

Captains to be Majors

B. S. Raju. Dated 4th June, 1943.

M. S. Chadha. Dated 19th June, 1943.

1st August, 1943

J. Brebner.

W. J. Virjin.

H. W. G. Staunton.

INDIAN LAND FORCES

INDIAN MEDICAL SERVICE—SECONDED TO INDIAN ARMY
 MEDICAL CORPS
 (Emergency Commissions)

Captain to be Major

Shiva Chandra Banerjee. Dated 24th August, 1943.

J. J. Barton. Dated 1st February, 1943.

W. Fleming. Dated 22nd May, 1943.
J. W. D. Goodall. Dated 5th August, 1943.
C. S. Gamble. Dated 20th October, 1943.

22nd October, 1943

D. W. Taylor. P. H. Addison.
J. Duffy. Dated 23rd October, 1943.
P. Das. Dated 3rd September, 1943.

Lieutenant to be Captain

T. B. W. Phillips. Dated 31st July, 1941.

PROMOTIONS

P. C. Lala. Dated 25th August, 1943.

4th September, 1943

K. C. Das. G. Bhattacharjee.
R. N. Chowdhury. H. D. Ghosal.
M. F. D'Silva. Dated 12th September, 1943.
S. V. Tungar. Dated 19th September, 1943.

22nd September, 1943

N. R. Gupta. N. Chatterjee.
K. Mujamdar. B. Banerjee.

23rd September, 1943

L. P. DeSouza. W. A. Lopcz.
A. M. Sharangapani. Dated 25th September, 1943.

28th September, 1943

M. J. Dutt. H. K. Das.

29th September, 1943

K. K. Lahiri. A. C. Das Gupta.
J. K. Roy. A. B. Sen Gupta.
H. C. Ghosh. Dated 30th September, 1943.
A. Kochugovindan. Dated 11th July, 1943.
B. N. Bhargava. Dated 30th August, 1943.

28th May, 1941

A. L. Sutherland. C. M. Burnie.
A. E. Stevens. J. D. Hardy.
D. Roberyson. A. D. Iliff.
R. A. Johnson. P. S. Fox.
H. W. T. Martin. A. W. B. Strahan.
J. R. Davidson. L. J. Michael.

W. G. Anderson.

PROMOTIONS

J. M. Flower. Dated 2nd July, 1941.

H. Flack. Dated 6th July, 1941.

6th August, 1941

B. A. Lamprell. A. B. Gilroy.

6th November, 1941

H. C. Duncan. C. S. F. Alkon.
R. H. Neeve. Dated 5th November, 1941.
E. G. Michelson. Dated 8th December, 1941.

(WITHIN INDIAN LIMITS)

Lieutenant to be Captain

V. L. Raja. Dated 14th September, 1943.

(WOMEN'S BRANCH)

Lieutenants to be Captains

Miss S. D. Chopra. Dated 16th September, 1943.
Miss C. Beemer. Dated 18th September, 1943.
Miss T. V. Sitalakshmi. Dated 21st September, 1943.

INDIAN MEDICAL SERVICE

(Permanent Commission)

The undermentioned officers (on probation) are confirmed with effect from the dates specified:—

10th January, 1939

Captain O. Walker. Captain E. L. Wilson.
Captain M. D. Black. Captain H. C. Rogers.
Captain G. J. H. Maud. Captain J. J. Woodward.
Captain I. D. Sutherland. Captain S. H. Heard.

12th March, 1939

Captain E. J. Somerset. Captain L. D. B. Frost.

12th May 1939

Captain J. A. M. Cameron. Captain R. J. McGill.
Captain C. C. Harvey. Dated 24th May, 1939.
Captain B. N. Bhandari. Dated 21st May, 1939.

Captain B. L. Kapur. Dated 22nd May, 1939.
Captain H. M. Kaul. Dated 26th May, 1939.
Captain A. K. Dev. Dated 31st May, 1939.
Captain M. Akram. Dated 2nd June, 1939.
Captain D. S. Raju. Dated 4th June, 1939.
Captain M. S. Chadha. Dated 19th June, 1939.
Captain C. S. Camble. Dated 20th October, 1939.
Captain S. Rameshwar. Dated 5th March, 1940.
Captain V. D'Arcy Blackburn. Dated 5th May, 1939.
Captain N. I. McLeod. Dated 5th April, 1940.
Captain F. J. O'Dowd. Dated 24th September, 1939.

RETIREMENTS

Major-General (Local Lieutenant-General) Sir Gordon Jolly, K.C.I.E., K.H.P. Dated 8th November, 1943.
Colonel C. A. Wood, M.C. Dated 18th May, 1943.
Lieutenant-Colonel J. C. John, O.B.E. Dated 22nd September, 1943.

RESIGNATION

The undermentioned officer is permitted to resign his commission:—

INDIAN LAND FORCES

INDIAN MEDICAL SERVICE—SECONDED TO INDIAN ARMY
MEDICAL CORPS

(Emergency Commissions)

Captain B. P. Das Gupta. Dated 26th June, 1943.

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